Title
Investigating the Clinical Utility of the Gastrointestinal Microbiome in Ulcerative Colitis

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Investigating the Clinical Utility of the Gastrointestinal Microbiome in Ulcerative Colits

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“Through adversity, there is redemption”

- HOWARD JONES, KILLSWITCH ENGAGE

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Investigating the Clinical Utility of the Gastrointestinal Microbiome in Ulcerative Colitis

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ABSTRACT

Despite centuries of research, the etiology of Ulcerative Colitis (UC; a chronic form of colonic inflammation) remains a mystery. As such, diagnosis is difficult, relying on clinical manifestations and resulting in an incredibly heterogeneous patient population. Furthermore, no cure (save colectomy) is available for UC, leading to a lifetime of therapies (many having variable efficacy; a consequence of UC patient heterogeneity). As UC prevalence rises, substantial need for enhanced therapies exists.

The gastrointestinal microbiome represents a promising avenue for improved treatment practices for UC. Being a diverse microbial community with substantial metabolic activity, opportunity exists for commensal microbes to influence host health, specifically the immune system. Indeed, several common colonizers of the mammalian gut regulate specific aspects of host immunity relevant to UC (such as Th17 and regulatory T-cell abundance, lymphocyte recruitment, and epithelial barrier function) through production of immunomodulatory metabolites. While UC was originally described as non-infectious diarrhea, studies demonstrating the potential efficacy of microbe-based treatments (i.e., probiotics) and the impact of microbes on animal models of UC suggest the microbiome contributes in a non-classical form of pathogenesis. Building on this, independent researchers found the gastrointestinal microbiome of UC patients to be less diverse and more compositionally variable compared to healthy people. Though these findings implicate the gastrointestinal microbiome in UC, questions remain regarding the therapeutic potential of gut microbes to improve patient outcomes.

This thesis addresses the clinical utility of the gastrointestinal microbiome in improving UC treatment. The therapeutic potential of microbiome manipulation was demonstrated using a murine model of UC and indicated gastrointestinal niches upstream of the colon harbor microbial activity associated with both disease induction and remission, suggesting patients might benefit from remodeling of microbial communities throughout the intestines. Additionally, a human study was conducted to demonstrate the utility of the microbiome with respect to improved stratification of UC patients. This work indicated discrete microbial states exist within the UC population, associate with symptom severity, and, via unique metabolic programming, differentially regulate T-cell activity. Together, this work highlights the microbiome as a resource for the development of both novel therapies and personalized treatment regimens for UC.

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CHAPTER 1

Introduction

Despite being first described over 150 years ago, the etiology of Ulcerative Colitis (UC), one of the main forms of Inflammatory Bowel Disease (IBD) and characterized by chronic, contiguous inflammation of the colonic mucosa, has continued to evade researchers (1, 2). As the true cause of UC remains unknown, diagnosis is primarily based on patient symptoms and clinical manifestation (3), resulting in a highly heterogeneous population of UC patients (2, 4, 5). Age of onset, symptom severity, frequency of extra-colonic manifestations, and disease progression are variable amongst UC patients and contribute to the difficulties in predicting patient outcomes and response to a given therapy (2-4, 6). Ultimately, colectomy represents the most effective treatments for severe pan-colitic disease and, despite having its own set of long-term costs and complications (7), approximately 30% of UC patients undergo surgery (6, 7). Given the high prevalence (ranging from 12 to 240 cases per 100,000 people) in North American and European countries, rising worldwide frequency, and the chronic nature of UC, a better understanding of both underlying disease mechanisms and patient heterogeneity could lead to improved quality of life through the development of novel therapeutic options and personalized treatment protocols while reducing the substantial medical costs ($6,200 to $11,500 annually per patient) and combined total economic burden (approximately $12 Billion annually in the United States) of this disease (4, 6, 8).

Due to the nature of UC, microbes had long been hypothesized to play a role in the pathogenesis of this disease (2, 9, 10). While microbial infection was originally thought to be the cause of UC, this notion was quickly dispatched due to a number of disease features including lack of both transmissibility and sustained efficacy of antimicrobial agents (2, 9). Though it is clear microbes do not drive UC in the classical sense of microbial pathogenesis, considerable evidence supporting a pathogenic role for microbes in the context of UC still remains. This is highlighted by multiple studies demonstrating the efficacy of therapies focused on correcting microbial imbalances in the gut (11-16). For example, oral supplementation with *Escherichia coli Nissle 1917* was shown by independent research groups to maintain disease remission in UC patients (11-13). Additionally, treatment with VSL#3 (a probiotic supplement containing eight bacterial species) was shown to induce disease remission, though this was a relatively small trial containing 34 patients and lacking a placebo controlled group (14). Antibiotic administration has also been shown to induce remission in more severe cases of UC (15, 16), though the benefit of antibiotic use in less severe patients is variable at best (6). Furthermore, several mouse models of colitis, including both genetic and chemically induced models, exhibit a dependency on microbial colonization of the gut and, in some case, select for a specific community of microbes capable of initiating disease when transferred to otherwise healthy animals (10). Extending on these observations, several independent research groups have identified specific microbial taxa that commonly colonize a healthy gastrointestinal tract, such as Segmented Filamentous Bacteria (SFB), *Bacteroides fragilis*, *Clostridium spp.*, and *Lactobacillus spp.*, as capable of regulating host immune function in a variety of manners, both pro- and anti-inflammatory (17-21). The immunoregulatory influence of these microbes impact many facets of host immune function related to UC including Th17 induction (SFB), expansion of intestinal regulatory T-cells (*B. fragilis* and *Clostridium spp.*), reduced lymphocyte recruitment (*Lactobacillus paracasei*), and improved intestinal epithelial barrier function (*Lactobacillus rhamnosus GG)* (17-21). In these cases, SFB-derived antigens, polysaccharide A from *B. fragilis*, short chain fatty acids resulting from microbial fermentation, chemokine-degrading lactocepin, and a 40-kDa protein secreted by *L. rhamnosus GG* were identified as the respective microbially-derived products responsible for immune modulation (18, 20-25). Finally, to further demonstrate the potential of commensal organisms to influence UC, supplementation with these microbes and/or metabolites was found to significantly influence disease outcome in several murine models of colitis (17-21, 23, 26). Combined, these studies provide substantial evidence that the gastrointestinal microbiome, defined as the complete community of microbes colonizing the gastrointestinal tract, and its associated cell-associated and –secreted products can play a significant role in the development and/or maintenance of UC.

As interest in the gastrointestinal microbiome and its role in immune homeostasis has grown, a number of research groups have investigated compositional changes in gut microbiota associated with UC (27-31). In each study, researchers observed a significant shift in the gross composition of gut microbial assemblages of UC patients, compared to that of healthy participants, highlighted by a significant reduction in bacterial diversity (27-31). Despite the observed depletion of commensal bacteria, specific microbial taxa enriched or depleted in the context of UC have yet to be consistently identified across multiple studies (27-31). These findings assert that, though consistently depleted in bacterial diversity, the gross composition of UC-associated dysbiotic gut microbiomes varies considerably amongst patients. This substantial heterogeneity in UC-dysbiosis is exemplified by the gradient of compositional dissimilarity in gut microbiomes when comparing UC patients to healthy participants, with subsets of UC-microbiomes being compositionally very similar to that of healthy microbiomes while others exhibit distinct community composiitons (28-31). These observations prompt the following important questions regarding the role of the microbiome in UC which, combined, form the topic of this thesis:

1) *Is gut microbiome manipulation a feasible therapeutic option for the treatment of UC?*
2) *Might clinical heterogeneity amongst UC-patient be explained by their associated differences in gut microbiome composition?*

To address the potential therapeutic benefit of targeted manipulation of the gastrointestinal microbiota in UC, a murine experiment investigating both the therapeutic and microbial impact of probiotic and/or regenerative stem-cell therapy in the context of chemically induced colitis was conducted, of which a detailed description can be found in Chapter 2. In brief, this study demonstrated that manipulation of gut microbiota via probiotic supplementation ameliorated signs of colitis in animals. Additionally, despite disease manifestation in the colon, shifts in bacterial community composition following both disease onset and probiotic-induced remission, while observed in all regions of the lower gastrointestinal tract of animals, were greatest in the ileum, suggesting a potential role for the ileal microbiome, which is located proximal to the mesenteric lymph nodes, in therapeutic efficacy in addition to that of the colon. Taken together, these findings evidence the role of the gastrointestinal microbiome in both driving and mitigating UC and, as such, the therapeutic potential of microbial manipulation in this context.

The influence of the gastrointestinal microbial community in human UC patients was then examined and its potential contribution to the clinical heterogeneity present in this patient population explored. Chapter 3 of this thesis comprehensively describes the findings of this study. In summary, a multi-omic approach to analyze microbiome structure, composition and function, in parallel with *in vitro* immune response, was utilized to determine whether discrete, microbially driven UC endotypes exist within humans and relate to clinical features of disease. Through in-depth analysis of this multi-omic data, UC patients were stratified into discrete, clinically relevant subsets characterized by distinct microbial states, differing both compositionally and metabolically, and exhibiting differential levels of disease severity. Furthermore, the immunomodulatory capacity of patient fecal water was assessed *in vitro* and found to differentially modulate immune activity based on microbially-defined patient subsets in a manner consistent with observed differences in clinical severity. This study suggest that, in addition to being promoted by the metabolic activity of gut microbes, UC may encompass multiple, clinically distinct disease states that can be distinguished based on specific microbial features of the gastrointestinal microbiome.

As a whole, the research described in this thesis establishes the significance of the gastrointestinal microbiome in UC not only with respect to disease initiation and progression but also in the context of improved patient stratification. By demonstrating both the therapeutic potential of microbiome manipulation and the clinical relevance of microbiome-based patient stratification, this work lays the foundation for future research exploring the microbial immunomodulatory mechanisms contributing to UC in discrete patient groups, an initial effort towards the ultimate goal of personalized treatment.

CHAPTER 2

Amelioration of DSS-induced murine colitis by VSL#3 supplementation is primarily associated with changes in ileal microbiota composition

Content in this chapter was modified from the following publication:

JS Mar, NA Nagalingam, Y Song, M Onizawa, JW Lee, and SV Lynch. Amelioration of DSS-induced murine colitis by VSL#3 supplementation is primarily associated with changes in ileal microbiota composition. *Gut Microbes* 5(4), 494-503

ABSTRACT

Inflammatory bowel diseases encompass gastrointestinal illnesses typified by chronic inflammation, loss of epithelial integrity and gastrointestinal microbiota dysbiosis. In an effort to counteract these characteristic perturbations, we used stem cells and/or a probiotic preparation in a murine model of Dextran Sodium Sulfate induced colitis to examine both their efficacy in ameliorating disease and impact on niche-specific microbial communities of the lower GI tract. Colitis was induced in C57BL/6 mice by administering 3% DSS in drinking water for 10 days prior to administering one of three treatment plans: daily probiotic (VSL#3) supplementation for 3 days, a single tail vein injection of $1x10^6$ murine mesenchymal stem cells, or both. Ileal, cecal and colonic sections were collected for microbiota and histological analyses. Microbiota profiling revealed distinct bacterial community compositions in the ileum, cecum and colon of control untreated animals, all of which were predicted *in silico* to be enriched for a number of discrete KEGG pathways, indicating compositional and functional niche specificity in healthy animals. DSS-treatment perturbed community composition in all three niches with ileal communities exhibiting the greatest change relative to control animals. Each treatment group exhibited specific alterations in microbiota composition in the lower GI tract, though disease scores were only improved in VSL#3-treated animals. The ileal microbiota were most profoundly altered in composition in this group of animals and characterized by significant Enterobacteriaceae enrichment compared with colitic mice ($P < 0.05$).

INTRODUCTION

Inflammatory Bowel Diseases (IBD) describe diseases of the gastrointestinal (GI) tract typified by chronic inflammation and ulceration of the mucosal and sub-mucosal layers. Ulcerative colitis (UC), one of the most common forms of IBD, manifests clinically as contiguous, superficial mucosal inflammation in the colon, originating at the rectum and moving towards the proximal colon as disease progresses (32). To date, the etiology of UC remains unknown, though several factors have been associated with disease development including immune dysfunction, risk alleles, environmental exposures and, more recently, compositional changes in the communities of bacteria that inhabit the gut (33).

The communities of microorganisms that inhabit humans (i.e., the microbiota) have garnered increasing interest with respect to their role in host immune development and regulation. Indeed recent studies have identified specific GI bacterial species that can promote both pro- and anti-inflammatory responses relevant to IBD (17-21). For example, the presence of Segmented Filamentous Bacteria (SFB) in the ileum, has been shown to induce Th17 cell proliferation in mice, while *Clostridium* species belonging to clades IV or XIV promote proliferation of anti-inflammatory T-regulatory cells (T-reg), thus indicating that the composition of the GI microbiota plays a role in defining the degree and tone of immune activation in mammalian systems (17, 19). This is all the more relevant given that both human patients and mouse models of UC are characterized by significant reductions in GI microbiota diversity and loss of key commensal species necessary for maintenance of immune homeostasis (27, 28, 34-38). More specifically, decreased relative abundance of potentially immunomodulatory mucosal-associated species such as *Faecalibacterium prausnitzii, Clostridium leptum* and *Clostridium coccoides* have been reported for UC patient samples (37-40). These organisms all produce short chain fatty acids (SCFA), which have established anti-inflammatory effects in a variety of animal colitis models (23, 40-42). Furthermore, previous studies have independently demonstrated the anti-inflammatory effects of SCFA producers such as *F. prausnitzii,* *Clostridium butyricum* and *Clostridium tyrobuturicum*, both *in vitro* and in a variety of animal models of colitis (43-45). Hence loss of SCFA-producing bacteria from UC patients is believed to represent at least one mechanism by which microbial dysbiosis contributes to the heightened immune activation associated with the disease. Chronic immune activation is also associated with loss of mucosal barrier integrity, a factor believed to further fuel induction of host immune responses by permitting microbes and microbial products to enter the circulation (46-48).

Though it is unclear whether microbiota or barrier function deficiencies play a more prominent role in UC, therapeutic strategies that target these primary dysfunctions (e.g., probiotic supplementation and/or adjunctive cell therapy) could prove efficacious. Small-scale trials of either probiotic supplementation or stem cell therapy for UC have demonstrated variable efficacy in diverse human populations and mouse models (12, 14, 49-51). However, despite it's emerging role as a key modulator of immune response, little is known regarding the effect of such potential therapeutics on the composition of the gut microbiota. Here we examine the impact of a microbial supplement (VSL#3) to re-establish appropriate microbiota composition, mesenchymal cell therapy to restore epithelial barrier integrity, or a combination of both therapeutic modalities in a murine Dextran Sodium Sulfate (DSS) model of UC. The primary purpose of this study was to determine the effect of such manipulations, both individually and collectively, on the GI microbiota and disease outcomes. We also sought to identify the nature and primary site of compositional changes in the GI microbiota that associate with disease resolution in an attempt to determine whether specific lower GI niches, including those closely associated with lymphoid tissue, may serve as target sites for microbiota restoration therapies.

RESULTS

Spatial organization of the murine lower GI microbiota.

Though mice are commonly used for modeling disease, no study to date has examined, at high-resolution, the spatial organization of the murine lower GI tract microbiota. Tissue samples obtained from the ileum, cecum and colon of control (CNTL) mice were used to identify niche-specific community characteristics and the specific bacterial taxa that exhibit region-specific colonization proclivities in healthy animals. Compared to the cecum and colon, the ileum of healthy animals exhibited significantly reduced microbial diversity (BH-corrected $p<0.05$, Fig. 1A) and a compositionally distinct microbiota (*Adonis* and *Envfit,* $p<0.001$, Fig. 1B). Members of the *Bacillaceae* and *Lactobacillaceae* families (specifically, the *Bacillus* and *Lactobacillus* genera) were significantly enriched in the ileum while members of the *Lachnospiraceae* family (including the *Clostridium* and *Coprococcus* genera) were amongst the microbiota members most significantly depleted (p-value < 0.05, q-value < 0.1). This finding was consistent irrespective of whether ileal microbiotas were compared to either the cecal or colonic microbiotas (Tables S1 and S2).

Although colonic microbiotas trended towards being more diverse than cecal communities, this finding did not reach significance (Fig 1A). Cecal and colonic communities though proximal, were compositionally distinct (*Adonis* and *Envfit,* $p<0.001$, Fig. 1B). Cecal communities, compared with that present in the colon, were characterized by significant relative enrichment of *Bradyrhizobium* and *Prevotella* genera and organisms with the capacity for sulfur reduction (e.g., *Desulfovibrio* and *Desulfonauticus* species). Compared to cecal microbiotas, colonic microbiotas were significantly enriched for members of the *Bacillus, Lactobacillus* and *Streptococcus* genera amongst others (p-value < 0.05, q-value < 0.1, Table S3).

Given the distinct relative taxonomic enrichments at each of these sites, we sought to better understand the implications of differential community composition in each respective niche in healthy animals. We therefore used the representative 16S rRNA sequences of organisms significantly enriched in each niche together with Phylogenetic Investigation of Communities by Reconstruction of Unobserved States (PICRUSt; http://picrust.github.io/picrust/), a bioinformatics software used to predict functional metagenomes from a marker gene survey (such as 16S rRNA gene profiling), to predict the microbial-encoded functions enriched at each site (ileum, cecum and colon) (52). Compared to the ileum, the cecal and colonic microbiotas were both predicted to be enriched for pathways involved in bacterial invasion of epithelial cells, Rig-I receptor signaling and D-amino acid metabolism (Fig. S1), indicating that, though the microbiotas profiled at these sites are compositionally distinct, the primary pathways enriched in both cecal and colonic communities are relatively consistent. In contrast, ileal communities were not significantly enriched for any specific pathways (Fig. S1), though it should be noted that the algorithm used to predict function did not consider relative abundance of individual taxa, but rather presence/absence data.

DSS treatment has greatest effect on ileal microbiota composition.

Overall, microbial community diversity did not significantly differ between DSS-treated and healthy animals within each GI region examined at the end of the study (Fig. 1A), perhaps due to the relatively mild colitis induced by this treatment. However, coordinate analyses indicated that DSS-treatment induced compositional changes in all three regions of the gut (*Adonis* and *Envfit,* $p<0.05$, Fig. 1B). To determine whether the magnitude of DSS-induced change in microbiota composition differed between GI regions, pairwise Canberra distances (a measure of dissimilarity between two communities where 0 = low dissimilarity and 1 = high dissimilarity) between DSS treated and untreated communities within each GI region were compared. The average Canberra distance between DSS treated and untreated microbial communities in the ileum was found to be significantly higher than that of both the cecum and colon (BH-corrected $p<0.05$, Fig. 1C). The change in ileal microbiota composition induced by DSS administration was characterized by a depletion of unclassified *Rikenellaceae* members coupled with an enrichment of *Clostridiaceae* members (specifically, *Clostridium spp.*; p-value < 0.05, q-value < 0.1, Table S4). Comparative *in silico* metagenomic predictions facilitated by PICRUSt analysis, indicated a predicted loss of pathways involving indole alkaloid, flavone, 12-, 14- and 16-membered macrolide and betalain biosynthesis as well as ether lipid metabolism in ileal communities of DSS treated animals (Fig. S1). The only functional category enriched in the ileum of DSS-treated animals involved transcription. This demonstrates DSS-induced colitis is associated with microbial community changes in all regions of the intestine, the most significant of which occurred in the ileum and exhibited parallel loss of specific community functions that could plausibly be involved in controlling community composition at that site.

Figure 1.

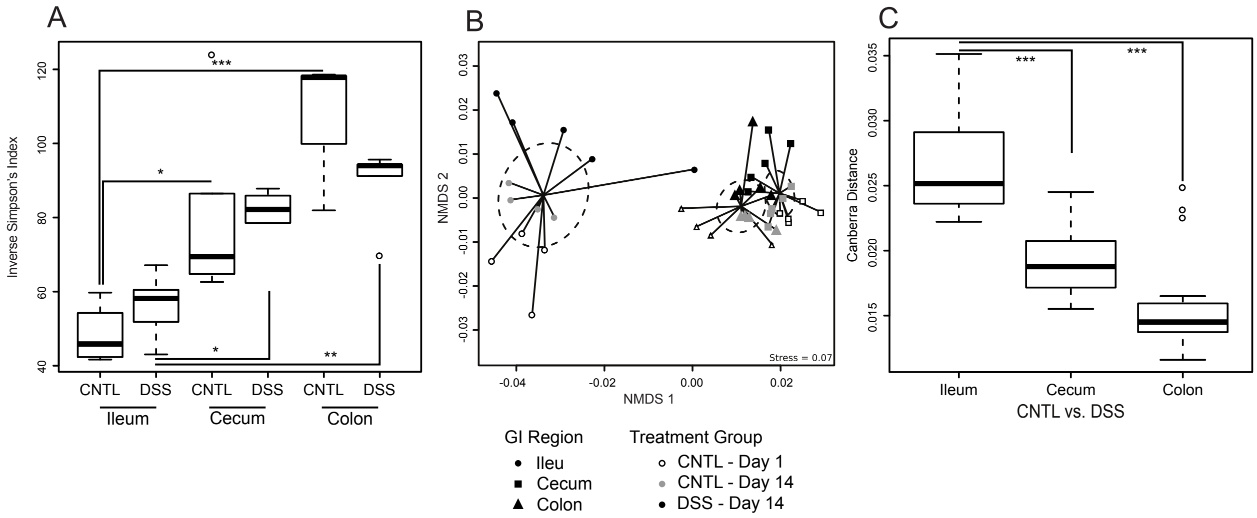


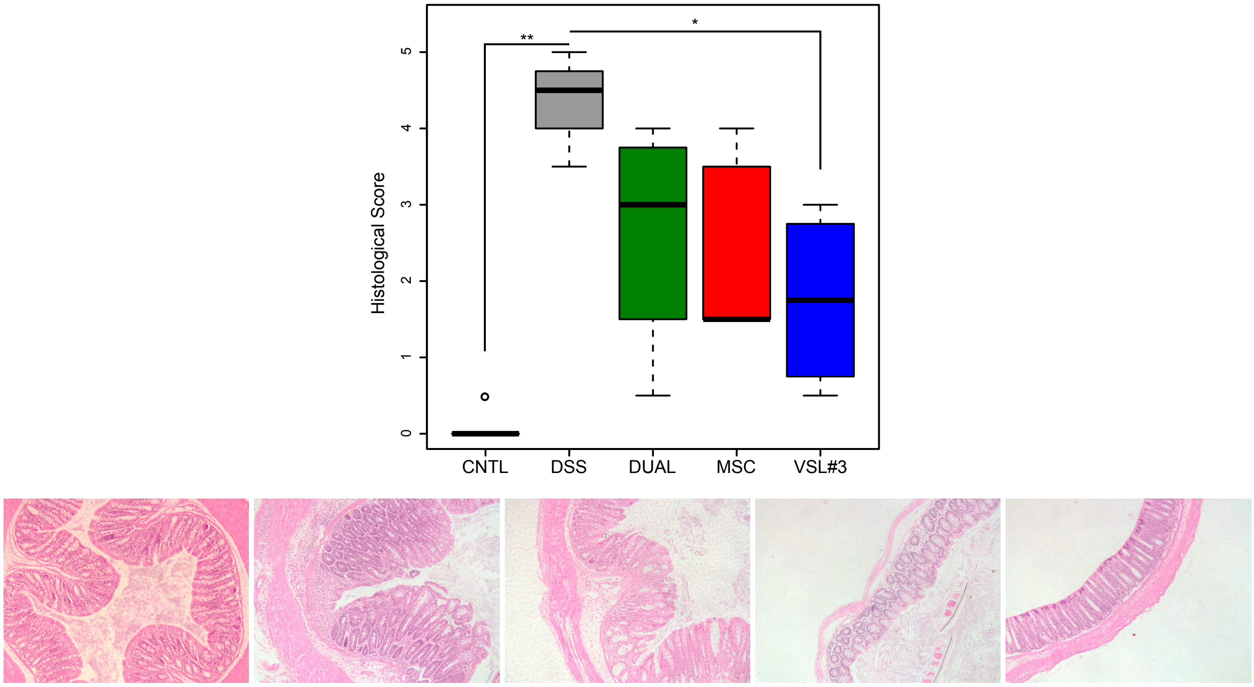
Figure 1. Region specific differences in microbial community composition.

A. Boxplot of microbial diversity of the ileum, cecum and colon in CNTL and DSS mice. **B.** Community composition of the ileum (circle), cecum (square) and colon microbiotas (triangle) represented by NMDS of pairwise Canberra distances. White and gray fill indicates CNTL samples from Day 1 and Day 14 respectively. Black fill indicates DSS samples from Day 14. Dashed ellipses represent the 95% confidence interval for the average ileal, cecal and colonic community coordinates. **C.** Boxplot of Canberra distances between CNTL and DSS-treated communities at each sampled site. (* BH-corrected p-value < 0.05, ** BH-corrected p-value < 0.01, *** BH-corrected p-value < 0.001).

Impact of MSC, VSL#3 and combined therapies on DSS-colitis.

At day 14 of the study, neutrophil infiltration and tissue damage was increased in the colon of DSS treated mice compared to untreated CNTL animals. This was reflected in the significantly increased disease score in DSS animals (BH-corrected $p<0.05$, Fig. 2). To investigate the affect of possible treatments for DSS-induced colitis on both disease status and the GI microbiota, regenerative (MSC) and probiotic (VSL#3) therapies were administered independently and in combination to three groups of animals. A separate but identical study using DSS-induced colitis and GFP-labeled MSCs was used to confirm that the MSCs successfully trafficked to the colitic gut in DSS-treated animals (Fig. S2). Histological analysis demonstrated that, while a single MSC treatment did reduce the disease score, the decrease was not significant, likely due to the broad range of disease scores across treated animals (BH-corrected $p = 0.055$, Fig. 2). The combination of regenerative and probiotic therapies resulted in a similar outcome with a wide degree of variability in disease scores and a non-significant trend towards reduction in disease severity compared to untreated, DSS animals (BH-corrected $p = 0.081$, Fig. 2). On the contrary, supplementation with probiotics alone (VSL#3) resulted in a consistent, significant reduction in disease severity score (BH-corrected $p<0.05$, Fig. 2).

Figure 2.



CNTL DSS DUAL MSC VSL#3

Figure 2. Colonic histology from mice in each treatment group at Day 14.

Boxplot of colonic histology scores for each treatment group at Day 14 along with representative images (100x magnification) of H&E stained colon tissue. (* BH-corrected p-value < 0.05, ** BH-corrected p-value < 0.01).

Effect of MSC, VSL#3 or combined therapies on the lower GI microbiota.

Since colitis has been associated with microbiota dysbiosis, we examined the bacterial communities in the ileum, cecum and colon of mice that received regenerative, probiotic, or combined therapies, as well as those present in DSS-treated and untreated, control animals. MSC-treated animals exhibited no significant difference in overall microbial community diversity at any site compared to DSS animals (Fig. 3A). Additionally, regenerative treatment was accompanied by little to no change in gross microbiota composition compared to DSS animals, regardless of GI region, as indicated by coordinate analysis (*Adonis* and *Envfit,* $p>0.05$, Fig. 3B). Consistent with this observation, there was a lack of significantly enriched or depleted bacterial taxa in the microbial communities of MSC mice compared to DSS mice, again, regardless of GI region examined (Tables S5-7). In contrast, VSL#3 supplementation either alone (VSL#3) or in combination with regenerative cell therapy (DUAL), was associated with a significant increase in ileal microbial diversity compared to DSS mice, though the extent of increased diversification was somewhat abrogated in the DUAL animals (BH-corrected $p<0.05$, Fig. 3A). In the cecum, only the VSL#3 group exhibited a significant difference in diversity from DSS animals (a decrease in diversity), while in the colon, no treatment modality elicited a significant difference in community diversity (BH-corrected $p<0.05$, Fig. 3A). Changes in diversity were largely driven by changes in community richness (taxa detected) rather than substantial changes in the evenness (relative distribution of taxa) of the communities (Fig. S3).

Beyond this VSL#3-associated change in microbial diversity, a distinct shift in the microbiota composition of both VSL#3 and DUAL animals compared to DSS animals in all three GI regions was observed (*Adonis* and *Envfit,* $p<0.05$, Fig. 3B). Using Permutational multivariate analysis, a significant relationship between variability in microbial community composition and treatment group (i.e., CNTL, DSS, DUAL, etc.) was evident at each GI region examined (*Adonis* and *Envfit,* $p<0.05$), further suggesting VSL#3 supplementation induced a significant shift in the microbiota assemblage. Consistent with the above findings, a comparison of mean Canberra distances demonstrated that, compared to the cecum and colon, ileal communities of VSL#3-treated animals exhibited the greatest distance from DSS-treated animals, indicating that this therapy elicited the greatest impact on the ileal microbiota composition (BH-corrected $p<0.05$, Fig. 3C). Further investigation into the discrete bacterial taxa that were enriched in the ileum following VSL#3 treatment revealed that, of the combined 113 OTUs significantly enriched in the ileum of either VSL#3 or DUAL animals compared to DSS animals, 52 significantly enriched OTUs were members of the *Enterobacteriaceae* family with many falling into unclassified genera (p-value < 0.05, q-value < 0.1, Fig. 4, Table S8-9). These results suggest VSL#3 supplementation, alone or in combination with stem cell therapy, following onset of DSS-induced colitis promotes development of a GI bacterial community distinct from that of DSS animals while regenerative stem cell therapy (MSC) does not. Furthermore, evidence suggests mice that exhibit significant reductions in disease severity scores following VSL#3 treatment demonstrate the most pronounced shift in ileal microbiota composition, a key site of immune modulation.

Figure 3.

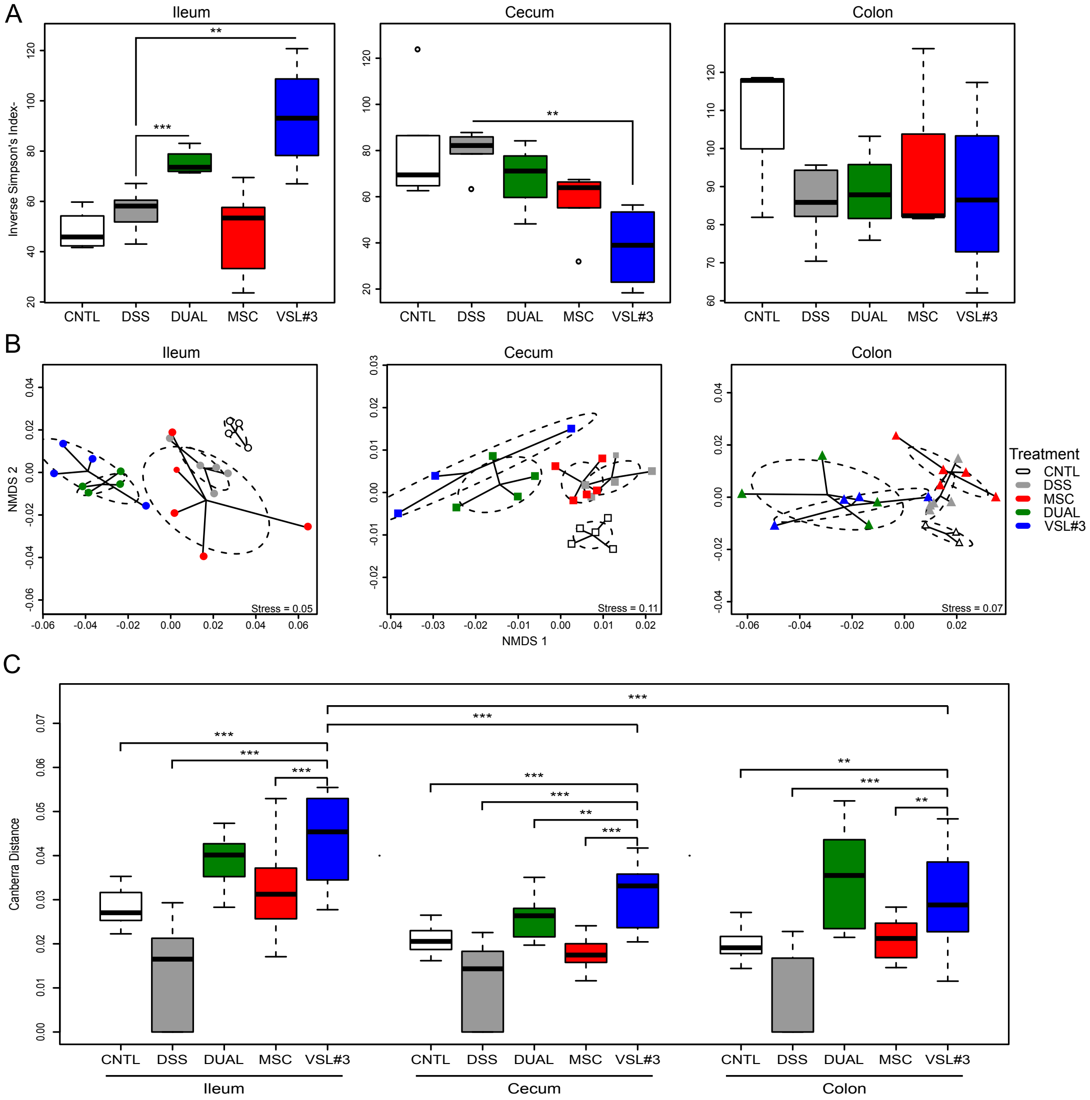


Figure 3. Impact of each treatment plan (CNTL, DSS, DUAL, MSC, or VSL#3) on ileal, cecal and colonic microbiota composition at Day 14.

(A) Boxplot of microbial diversity in the ileum, cecum and colon for all treatment groups. **(B)** NMDS of pairwise Canberra distances between treatment groups at Day 14 for each GI region examined. Dashed ellipses represent the 95% confidence interval for the average coordinate of each treatment group. **(C)** Boxplot of pairwise Canberra distances between each indicated treatment group compared and the DSS treatment at Day 14 for each GI region examined. (* BH-corrected p-value < 0.05, ** BH-corrected p-value < 0.01, *** BH-corrected p-value < 0.001).

Figure 4.

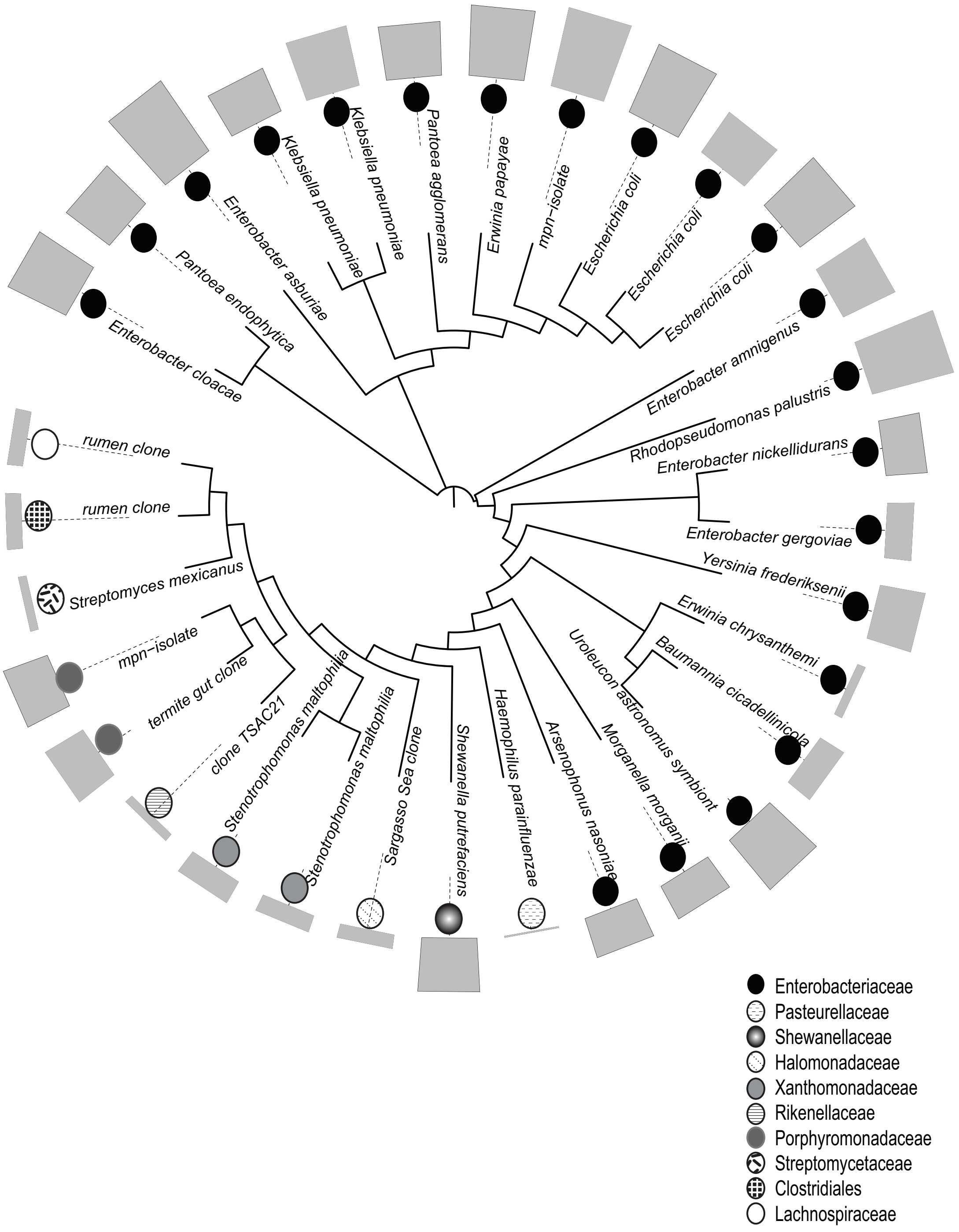


Figure 4. Dendrogram of top 32 taxa significantly enriched in the ileum of VSL#3 animals vs. DSS animals.

Grey bars represent magnitude of change in relative abundance across treatment groups. (p-value < 0.05, q-value < 0.1).

DISCUSSION

DSS has previously been associated with changes in both the cecal and colonic microbiota (36, 53). However, the findings reported here are the first to document changes in three regions of the lower intestine upon DSS treatment. Past studies have focused primarily on the colon, as it represents the main site of inflammation in murine models of UC. The terminal ileum, despite its proximity to lymphoid nodules and the proven capacity of microbes at this site to influence immune responses including those associated with UC, has been largely overlooked in murine colitis models (54, 55). In this study, we found that the ileal microbiota exhibits the greatest degree of compositional change following DSS treatment (compared to the cecum and colon). These compositional changes were predicted to result in a depletion of indole alkaloid, betalain, and 12-, 14- and 16-membered macrolide biosynthesis capabilities at this site, molecules which have previously been shown to contribute to improved epithelial barrier function via both immunomodulatory and antimicrobial effects (56-58). Loss of ileal barrier function associated with depletion of these species and their products may allow for increased translocation of microbial-derived, pro-inflammatory molecules whose effects, when combined with colonic dysbiosis, may manifest as overt, colonic inflammation. It is also possible that translocation of these ileal species and/or their products to the colon prevent symptoms at this downstream site. It is important to note that, while PICRUSt is a relatively robust metagenomic prediction tool, it is entirely dependent on the quality of the reference database used and is therefore incapable of accounting for strain variations present in a given community (52). At the very least, these results warrant further investigation into the role of the ileal microbiota in DSS-induced colitis.

In addition to examining the impact of DSS on ileal, cecal and colonic microbiota, we also assessed the impact of regenerative and probiotic therapies on disease recovery and GI microbial community composition. In our study, a single injection of MSC did not result in improved recovery from DSS-induced colitis, nor were there consistent or statistically significant changes in the microbiota of any region examined as a result of MSC treatment. This was perhaps due to the fastidious nature of the anti-inflammatory capabilities of MSC.(59) Since MSC were grown via traditional methods (i.e., in a cell culture plate) rather than using the suspended drop method described more recently by Bartosh el at., the anti-inflammatory properties of the MSC's used in this study may be reduced, leading to a diminished ability to curb DSS-induced inflammation.(59) Interestingly, microbial changes observed in the DUAL treatment communities resembled that of the VSL#3 group. Due to the lack of community changes associated with MSC treatment, the change in microbial composition observed in the DUAL treatment group is likely due to the effects of VSL#3 rather than the MSC. Although these changes were associated with a reduction in inflammation compared to DSS mice, the results were not statistically significant (BH-corrected p = 0.081). Bacterial supplementation therapy, in the absence of regenerative therapy, was the only treatment plan observed in this study design to significantly improve recovery from DSS induced colitis. Furthermore, this improved recovery was associated with substantial change in the composition of the GI microbiota. Previously published studies have associated VSL#3 supplementation with changes in the colonic microbiota through the fingerprinting method of restriction fragment length polymorphisms.(35) In addition to corroborating these finding, we reported VSL#3 treatment to be linked to significant microbiota changes in the terminal ileum as well. Compared to the cecum and colon, the ileal microbiota exhibited the most dramatic response to not only DSS administration, as mentioned above, but also to VSL#3 administration. This suggests the ileal community may have an immunomodulatory role in both the onset of and recovery from DSS induced colitis. Similar to the previously discussed hypothesis regarding a potential role for the ileal microbiota in DSS-induced colitis, probiotic-induced changes in the ileal microbiota may promote recovery from DSS-induced colonic inflammation by both producing a milieu of metabolites that flow downstream to the colon, enriching for a more anti-inflammatory microbial community, and by reducing translocation of pro-inflammatory molecules via promotion of improved barrier function in the ileum.

A striking observation in our study was that the large change in the ileal microbiota composition of VSL#3 treated animals was characterized by an enrichment of Enterobacteriaceae members relative to DSS animals, suggesting that members of this family that reside in the ileum may produce products that protect against colonic inflammation. Frank *et al.* observed a similar, though not statistically significant, trend in the colonic tissue of healthy controls compared with both CD and UC patients (28). Though the Enterobacteriaceae family is traditionally associated with development of disease, as it contains many well-described pathogenic species, some of these members confer beneficial and protective effects to the host when present in specific microbial community contexts. Numerous studies have demonstrated the beneficial effects of *E. coli* strain Nissle 1917, especially with respect to UC (11-13, 60). This concept is also exemplified by the Clostridium genus, which contains both pathogens, e.g., Clostridium difficile (which is highly virulent in the context of a depleted microbiota), as well as beneficial SCFA-producing members, such as C. leptum and C. coccoides, typically present in a diverse healthy gut consortium (61). It is also possible that the ileal microbiotas of the VSL#3 mice recover via successive waves of microbial outgrowth, a well described ecological process known as secondary succession, and that observing this community at repeated time points following VSL#3 administration would yield information on this dynamic process and the influence of VSL#3 as a potential inoculum that influences community reassembly kinetics following disturbance. As such, further investigations into the dynamics of ileal microbiota recovery following both DSS administration and VSL#3 therapy may be necessary.

Emerging evidence points to the gut microbiota as playing a significant role in modulating immune responses. Given our data, the microbial community of the ileum would appear to be an ideal target for examination, particularly given previous evidence for interactions between microbes, microbial products, and host immune cells at this site (62-64).

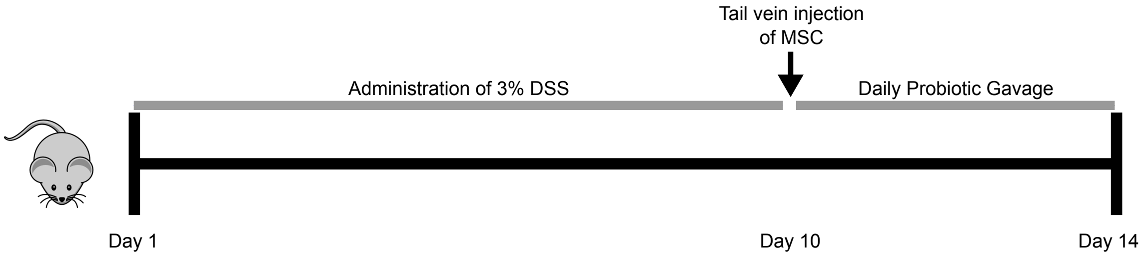
This study, to our knowledge, is the first to examine the ileal microbiota composition in a murine model of therapeutic intervention for UC. Our observations suggest the microbial contents of the ileum may play a much larger role in both onset and amelioration of DSS-induced UC than previously appreciated. We anticipate that future investigation into the differences in ileal metabolic profiles between healthy, diseased and recovering animals may identify key metabolic functions necessary to prevent and ameliorate disease. Combined with the data in this study, such an approach could identify specific microbial species that encode crucial beneficial functions which form the basis for development of more expansive probiotic therapies for a variety of GI inflammatory diseases.

MATERIALS & METHODS

Animals

All animal experiments were conducted in accordance with the University of California, San Francisco, Institutional Animal Care and Use Committee (IACUC) guidelines (Approval #AN092079). Eight week old female C57BL/6 were housed under 12 hour light/dark cycle conditions in the University of California, San Francisco (UCSF) animal facilities and fed a standard diet (PicoLab, Mouse Diet 20) for the duration of the study. All mice (n=40) were initially housed together (5 animals per cage) to control for cage effect prior to being randomly divided into five experimental groups, four of which received Dextran Sodium Sulfate (DSS; 3% solution in drinking water) for 10 days to induce colitis. Once treatment groups were assigned, animals were re-caged (5 mice per cage) based on assigned treatment group to prevent coprophagy between groups. Three of the DSS-treated groups received the following treatment modalities: VSL#3(VSL#3, n=5), mesenchymal stem cells (MSC, n=5), or VSL#3 + mesenchymal stem cells (DUAL, n=5). The fourth DSS-treated group received no intervention (DSS; n=10). The additional fifth group of animals received neither DSS nor any therapeutic intervention and acted as untreated controls (CNTL, n=15). Following colitis induction (Day 10), DSS administration was halted and mice in the VSL#3, MSC and DUAL groups received the following interventions respectively: daily oral supplementation with $9x10^8$ CFUs in 100ul sterile water (VSL#3); a single tail vein injection of $1x10^6$ murine mesenchymal stem cells in 100µl PBS on Day 10 (MSC) or a combination of both treatments (DUAL; Fig. 5). VSL#3 concentrations were selected based on previous studies investigating the effects of VSL#3 treatment in a variety of murine IBD models.(35, 65, 66) Mesenchymal stem cell concentrations were adapted from previous studies examining the therapeutic efficacy of intravenous administration of mesenchymal stem cells in murine models of colitis and acute lung injury.(67, 68) Following induction of colitis, mice did not receive any form of treatment (i.e., analgesic) other than the described probiotic and/or mesenchymal stem cell treatment plan as analgesics have previously been show to directly impact inflammatory responses in DSS induced colitis.(69) Because additional forms of treatment were not used to minimize pain and discomfort, we were required to euthanize all animals 96 hours post colitis development. To provide control data for comparison, CNTL mice (n=5 per time point) were euthanized and sampled on days 1, 10, and 14, while DSS mice (n=5 per time point) were euthanized on days 10 and 14. All MSC, VSL#3, and DUAL mice were euthanized on Day 14. Samples collected from each animal included terminal ileum (1cm proximal to the cecum), cecum (divided transversely and stored as two separate samples), and proximal colon. All samples were added to RNA*later*, prior to storage at -80°C for analysis. Additional colonic samples were obtained, proximal to the initial sample site for microbiota analyses, and were preserved in paraformaldehyde for histological analyses.

Figure 5.



Experimental Treatment Groups:

CNTL: Control group (n = 15, 3 cages)
DSS: Received DSS for 10 Days (n = 10, 2 cages)
MSC: Received MSC injection (1x10^{6}) following 10 Days of DSS (n = 5, 1 cage)
VSL#3: Received daily gavage of VSL#3 (9x10^{8}) for 4 days following 10 Days of DSS (n = 5, 1cage)
DUAL: Received both MSC and VSL#3 following 10 Days of DSS (n = 5, 1 cage)

Figure 5. Outline of experimental design.

Drinking water was replaced with a 3% DSS solution for 10 d to induce colitis in DSS, VSL#3, MSC and DUAL mice (CNTL mice were given regular drinking water). MSC mice received a single tail vein injection of 1x106 mouse mesenchymal stem cells suspended in 0.1ml PBS on Day 10. VSL#3 mice received VSL#3 (5x106 total cells, daily) via oral gavage daily from Day 10 to Day 14. DUAL mice received both the single mesenchymal stem cell injection as well as daily VSL#3 supplementation. On Days 1, 10, and 14, five CNTL mice were euthanized. Five DSS mice were euthanized on Days 10 and 14. All MSC, VSL#3, and DUAL mice were euthanized on Day 14.

Stem Cell Trafficking

Eight-week-old C57BL/6 mice (n=5) were administered 3% DSS in drinking water for 10 days until onset of colitis. Control animals (n=5) were provided regular drinking water. On day 10, DSS administration was halted and three animals in each group received a single tail vein injection of 1×10^6 green fluorescent protein-labeled mouse mesenchymal stem cells (MSC-GFP; Health Science Center at Texas A&M University, TX) suspended in 100µl PBS. Following our original experimental design, all animals were euthanized on day 14 and their GI tracts harvested for fluorescent imaging using a charge-coupled device camera [*in vivo* imaging system (IVIS®); Xenogen Corp., CA] to permit visualization of stem cell localization in colitic compared to non-colitic animals.

Necropsy and Histology

Sections of the GI tract were fixed in formalin solution overnight before dehydration in 70% ethanol. Samples were sectioned and stained using haemoxylin and eosin (H&E). Disease score was assessed according to the histological scoring parameters described by T. Ishikura *et al.*(70) Briefly, a score ranging from 0 (healthy) to 6 (extensive inflammation and damage) was determined by combining a measure of tissue damage (0-3) and the level of inflammatory cell infiltration (0-3). Two researchers independently scored de-identified samples, and mean scores were calculated.

Nucleic Acid Extraction

Terminal ileum, cecum and colon samples stored at -80°C in RNA*later* were thawed on ice prior to extraction of nucleic acids. DNA was extracted from individual samples using a combination of bead beating and the commercially available AllPrep kit (Qiagen, CA) as we have previously described.(71)

PhyloChip Processing

Total DNA extracted from terminal ileum, cecum, and colon samples was used as template for 16S rRNA gene amplification as previously described.(72) PCR amplification was verified on a 1% TBE agarose gel then purified using the QIAquick Gel Extraction kit (Qiagen, CA). A total of 500ng of purified PCR product per sample was then fragmented, biotin-labeled, and hybridized to the G2 16S rRNA PhyloChip (Affymetrix, CA) as previously described.(17) Washing, staining, and scanning of arrays were conducted according to standard Affymetrix protocol.(17) Background subtraction, detection, taxon quantification criteria and array normalization was performed as previously described.(17, 73) Stage 1 thresholds were adjusted, based on quantitative standards to the following: $rQ1 \geq 0.38$, $rQ2 \geq 0.57$, $rQ3 \geq 0.82$. All microbiota data reported in this paper has been deposited in the Gene Expression Omnibus (GEO) database, www.ncbi.nlm.nih.gov/geo (accession no. GSE56137).

Statistical Analysis

Much of the statistical analyses were performed as we have previously described using custom scripts and packages in the R statistical environment to examine differential aspects of gross and detailed taxonomic structure and function as well as to determine correlations (both linear and non-linear relationships) between community structure, taxonomic relative abundance and disease variables measured in this study.(72, 74) Community richness was defined as the total number of Operational Taxonomic Units (OTU) in a sample that had a pf-value ≥ 0.93 and had passed Stage 1 filtering.(73, 75) Evenness was calculated using Pielou's index (j): $j = H(s) / H(max)$, where $H(s)$ = Shannon-Wiener diversity index and $H(max)$ = the theoretical maximum value for $H(s)$ if all species in the sample were equally abundant.(76) Diversity was calculated using Inverse Simpson's index: $1/D = \sum (n/N)^2$ where D = Simpson's index; n = the total number of organisms of a particular species; and N = the total number of organisms of all species. All indices were calculated using the *Vegan* (http://vegan.r-forge.r-project.org/) package in the R statistical environment. Log-transformed array-reported fluorescence intensities were used to calculate weighted, pairwise Canberra distance values using the following equation:

$$D_{jk} = (1/NZ) * \Sigma^{\text{All Non-Zero OTUs}}(|x_{ij}-x_{ik}|/(x_{ij}+x_{ik}))$$

Where j = sample 1, k = sample 2, NZ = the number of OTUs with fluorescence intensities greater than 0 in at least one sample, x = fluorescence intensity, and i = OTU. Briefly, Canberra distance is the average absolute difference in OTU abundance (normalized to combined OTU abundance) for OTUs present in the communities being compared. These values were used for visualization of community compositional dissimilarity using non-metric multi-dimensional scaling (NMDS). Permutational multivariate analysis of variance using the calculated distance matrix was used to determine whether relationships existed between microbiota composition and measured variables, such as experimental treatment conditions, GI location, or disease score, using *Envfit* and *Adonis* as we have previously described.(72, 74, 77) Significant between-group differences in community indices (e.g., diversity of CNTL vs. DSS) were determined using the ANOVA statistical test followed by pairwise, two-tailed *t*-tests adjusted for FDR.(78) Significant between-group differences in taxon relative abundance were determined using a two-tailed *t*-test, adjusted for false discovery using *q*-values, as we have previously described.(72, 74, 77) Taxa exhibiting significant enrichment (p-value < 0.05, *q*-value < 0.1) were ranked based on their magnitude of change in relative abundance.

Predicted community metagenome analyses.

Phylogenetic Investigation of Communities by Reconstruction of Unobserved States (PICRUSt; http://picrust.github.io/picrust/), a bioinformatics software used to predict functional metagenomes from a marker gene survey (such as 16S rRNA gene), was used to generate *in silico* metagenomes for data generated in this study.(52) First, 16S rRNA sequences of OTUs significantly enriched in each comparison group (e.g., Ileal CNTL vs. Ileal DSS) were obtained from the GreenGenes database (http://greengenes.secondgenome.com/downloads/database/13_5) using a custom script written in Python. Retrieved FASTA 16S rRNA sequence files were imported into QIIME (http://qiime.org/) to generate an OTU table, through a closed-referenced OTU-picking protocol to create biom-formatted OTU tables. These OTU tables were then subjected to PICRUSt analysis and grouped into corresponding KEGG pathways using the KEGG database (http://www.genome.jp/kegg/pathway.html). Results of between-group comparisons were visualized using a heat map constructed using a custom script written in R, to indicate, based on presence-absence data, the biological functions enriched in each respective group. The custom pipeline developed to analyze and visualize this data is open source and available at GitHub (https://github.com/alifar76/PHoP).

SUPPLEMENTARY FIGURES & TABLES

Figure S1.

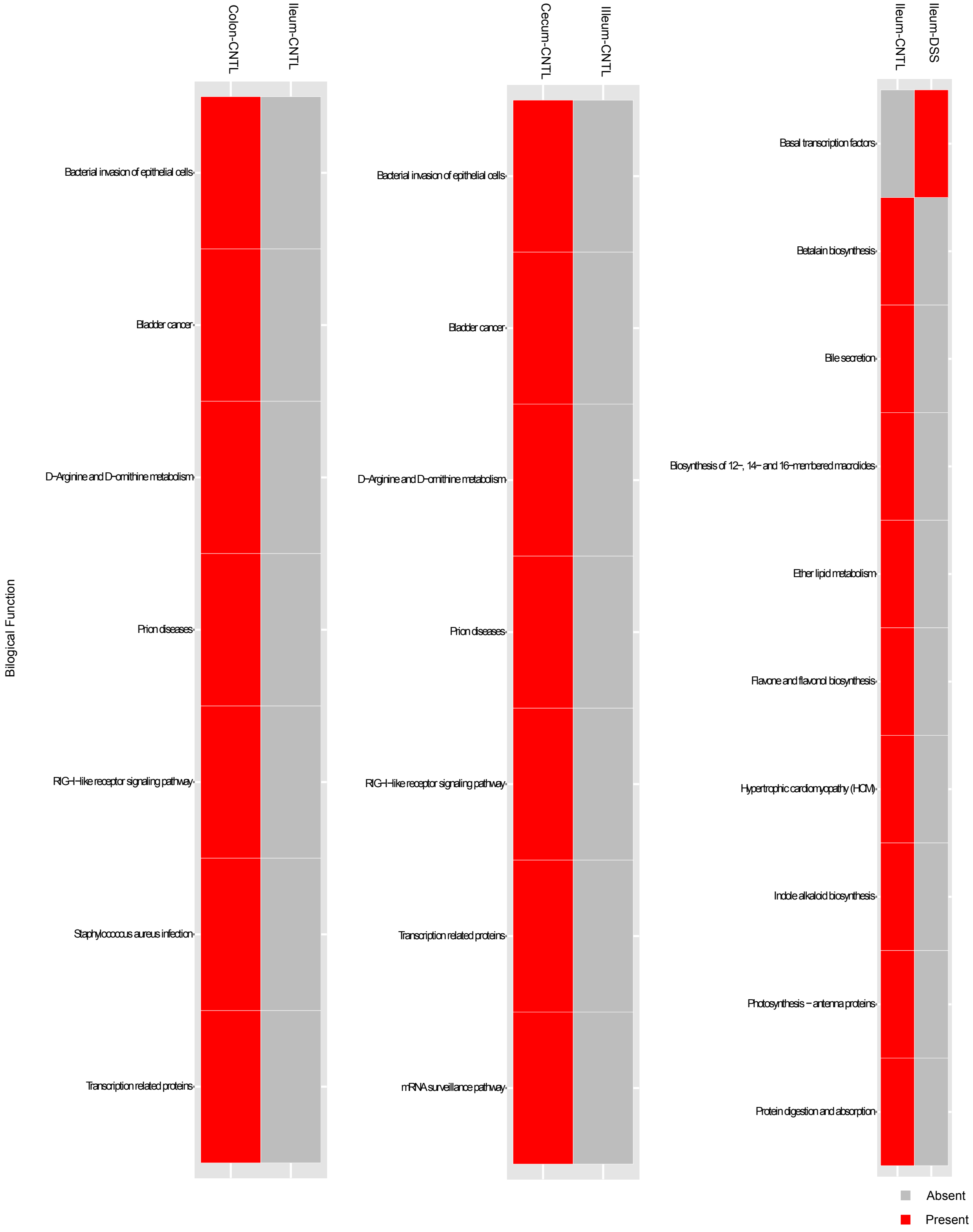


Figure S1. Heat maps depicting predict KEGG pathways enriched between different comparison groups.

Figure S2.

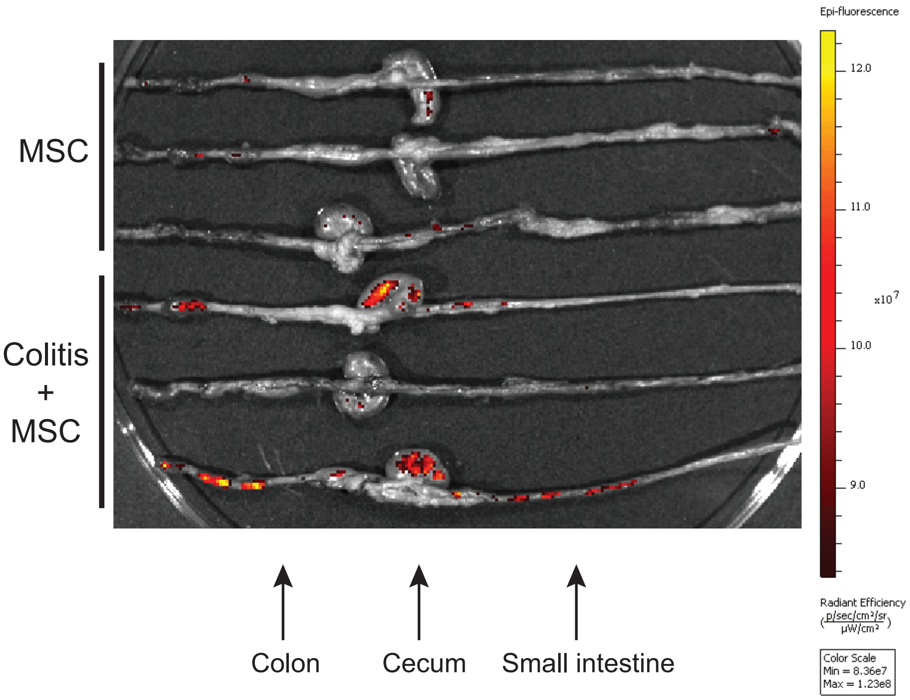


Figure S2. More gfp- labeled MSCs traffics to the intestine of colitic mice than healthy animals.

Figure S3.

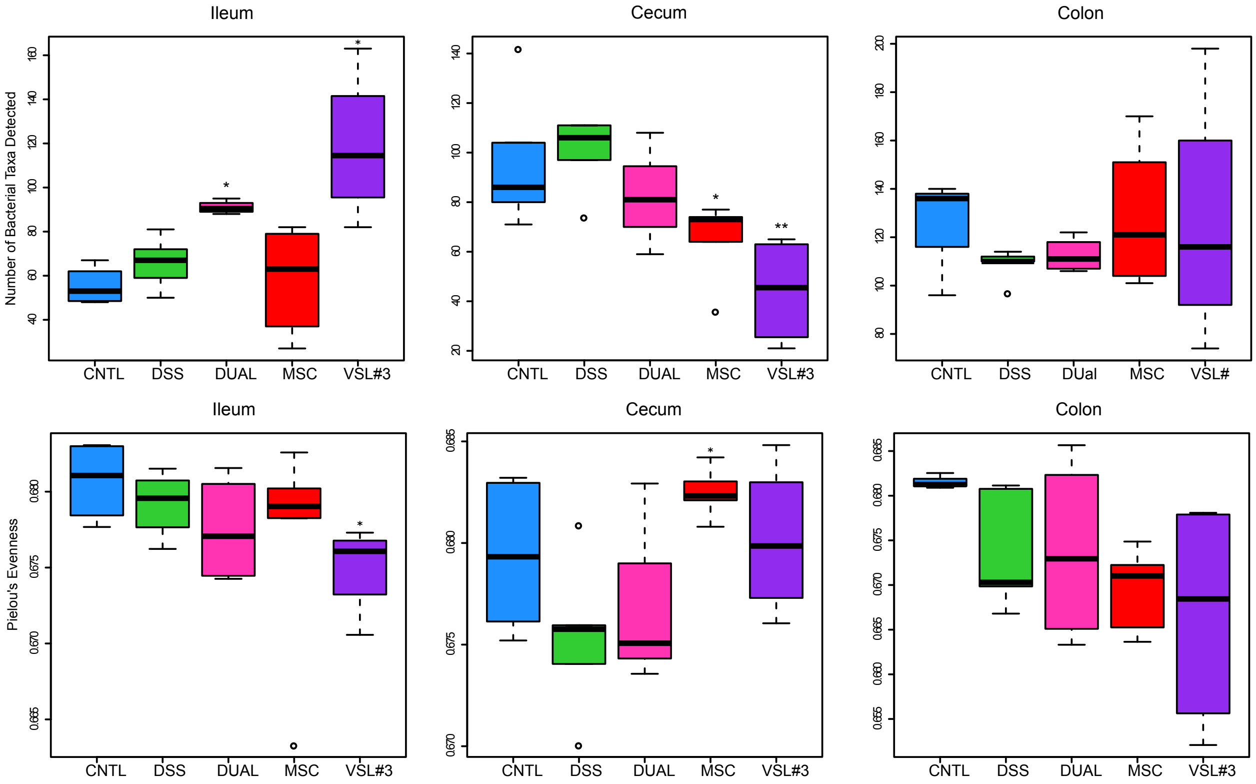


Figure S3. Community Richness (# of OTUs present) and Evenness (relative distribution of OTUs) in the ileum, cecum and colon from each treatment group.

Table S1. Significantly enriched bacterial OTUs - Control Ileum vs. Control Colon. Table sorted by Fold Change. T-test p-value < 0.05, q-value < 0.16

OTU	Phylum	Class	Order	Family	Genus	Fold Change (Ileum / Colon)	pvalue	qvalue
10989	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	Clostridium	2.1545	0.0001	0.0001
5791	Firmicutes	Bacilli	Bacillales	Bacillaceae	Salinibacillus	1.8781	0.0001	0.0001
6624	Firmicutes	Bacilli	Turicibacterales	Turicibacteraceae	Turicibacter	1.8106	0.0012	0.0008
5524	Firmicutes	Bacilli	Bacillales	Alicyclobacillaceae	Alicyclobacillus	1.8004	0.0005	0.0003
6646	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.7895	0.0000	0.0000
6711	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	1.7558	0.0001	0.0001
5046	Verrucomicrobia	Verrucomicrobiae	Verrucomicrobiales	unclassified	sfH	1.7518	0.0000	0.0000
6900	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.7182	0.0295	0.0098
1083	Actinobacteria	Actinobacteria	Bifidobacteriales	Bifidobacteriaceae	Bifidobacterium	1.7164	0.0080	0.0033
1074	Actinobacteria	Actinobacteria	Actinomycetales	Streptomycetaceae	Streptomyces	1.7087	0.0091	0.0037
6997	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.6658	0.0001	0.0001
6488	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.6629	0.0004	0.0003
5730	Spirochaetes	Spirochaetes	Spirochaetales	Spirochaetaceae	IE043	1.6431	0.0033	0.0016
11099	Tenericutes	Erysipelotrichi	Erysipelotrichales	Erysipelotrichaceae	PSB-M-3	1.6346	0.0000	0.0001
5829	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.6290	0.0008	0.0005
8942	Proteobacteria	Alphaproteobacteria	Rhodospirillales	Acetobacteraceae	Asaia	1.6240	0.0147	0.0056
6959	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.6112	0.0005	0.0004
7300	Proteobacteria	Alphaproteobacteria	Rhodospirillales	Rhodospirillaceae	unclassified	1.6041	0.0003	0.0002
6502	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.5934	0.0217	0.0076
6633	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.5880	0.0000	0.0000
5857	Firmicutes	Bacilli	Bacillales	Bacillaceae	Geobacillus	1.5815	0.0001	0.0001
7548	Bacteroidetes	Bacteroidia	Bacteroidales	Porphyromonadaceae	unclassified	1.5759	0.0002	0.0002
2747	Proteobacteria	Gammaproteobacteria	Oceanospirillales	ZA3412c	unclassified	1.5659	0.0001	0.0001
6235	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.5621	0.0001	0.0001
5947	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.5588	0.0001	0.0001
5835	Firmicutes	Bacilli	Bacillales	Paenibacillaceae	Paenibacillus	1.5531	0.0033	0.0016
9787	Proteobacteria	Alphaproteobacteria	Rhizobiales	Bradyrhizobiaceae	Bradyrhizobium	1.5529	0.0155	0.0058
6544	Firmicutes	Bacilli	Bacillales	Planococcaceae	Planomicrobium	1.5500	0.0001	0.0001
9724	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	Clostridium	1.5432	0.0274	0.0093
6599	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	1.5422	0.0284	0.0095
5629	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.5389	0.0002	0.0001
8924	Bacteroidetes	Flavobacteria	Flavobacteriales	Flavobacteriaceae	unclassified	1.5319	0.0217	0.0076
6003	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.5292	0.0092	0.0037
6387	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.5283	0.0414	0.0133
6913	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	1.5269	0.0013	0.0008
9826	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	Clostridium	1.5257	0.0001	0.0001
3814	Firmicutes	Clostridia	MBA08	unclassified	sfA	1.5250	0.0002	0.0002
6583	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.5236	0.0018	0.0010
5839	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	1.5227	0.0025	0.0013
1243	Actinobacteria	Actinobacteria	Actinomycetales	Streptomycetaceae	Streptomyces	1.5186	0.0004	0.0003
8114	Proteobacteria	Alphaproteobacteria	Rhodospirillales	Rhodospirillaceae	unclassified	1.5119	0.0026	0.0013
5428	Firmicutes	Bacilli	Bacillales	Paenibacillaceae	Paenibacillus	1.5081	0.0025	0.0013
6379	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.5017	0.0042	0.0019
6923	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	1.4897	0.0050	0.0022
10836	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	Clostridium	1.4750	0.0004	0.0003
9655	Tenericutes	Mollicutes	Acholeplasmatales	Acholeplasmataceae	Candidatus Phytoplasma	1.4713	0.0020	0.0011
467	Lentisphaerae	Lentisphaerae	Victivallales	Victivallaceae	unclassified	1.4653	0.0001	0.0001
6568	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.4478	0.0163	0.0060
5401	Firmicutes	Bacilli	Bacillales	Paenibacillaceae	Paenibacillus	1.4454	0.0003	0.0002
5444	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.4453	0.0013	0.0008
6298	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.4438	0.0000	0.0000
5389	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.4388	0.0014	0.0008
5680	Spirochaetes	Spirochaetes	Spirochaetales	Spirochaetaceae	Spirochaeta	1.4312	0.0028	0.0014
5817	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.4276	0.0003	0.0002
5842	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.4264	0.0024	0.0012
6408	Firmicutes	Bacilli	Bacillales	Alicyclobacillaceae	Alicyclobacillus	1.4253	0.0076	0.0032
10877	Cyanobacteria	Chloroplast	Streptophyta	unclassified	sfA	1.4206	0.0025	0.0013
5628	Firmicutes	Bacilli	Bacillales	Paenibacillaceae	Paenibacillus	1.4194	0.0018	0.0010
5961	Firmicutes	Bacilli	Bacillales	Bacillaceae	Geobacillus	1.4176	0.0012	0.0008
1041	AD3	ABS-6	unclassified	unclassified	sfA	1.4138	0.0053	0.0023
6229	Spirochaetes	Spirochaetes	Spirochaetales	Spirochaetaceae	Treponema	1.4126	0.0001	0.0001
6478	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	1.4051	0.0169	0.0062
9918	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	1.4049	0.0000	0.0000
9995	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Ruminococcus	1.4037	0.0147	0.0056
1914	Bacteroidetes	Sphingobacteria	Sphingobacteriales	Flammeovirgaceae	Roseivirga	1.4036	0.0006	0.0004
6572	Firmicutes	Bacilli	Bacillales	Bacillaceae	Geobacillus	1.4016	0.0027	0.0013
2203	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	1.3990	0.0114	0.0045
6042	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.3989	0.0041	0.0019
3509	Firmicutes	Clostridia	Thermoanaerobacterales	Thermoanaerobacteraceae	unclassified	1.3985	0.0016	0.0009
6726	Firmicutes	Bacilli	Bacillales	Bacillaceae	Geobacillus	1.3956	0.0024	0.0012
6947	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.3946	0.0012	0.0008
2011	Proteobacteria	Gammaproteobacteria	Pseudomonadales	Pseudomonadaceae	Pseudomonas	1.3912	0.0013	0.0008
88	Actinobacteria	Actinobacteria	Bifidobacteriales	Bifidobacteriaceae	Bifidobacterium	1.3909	0.0014	0.0009
6068	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	1.3872	0.0044	0.0020
10599	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Clostridium	1.3859	0.0000	0.0000
6233	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.3831	0.0038	0.0018
10012	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	1.3753	0.0482	0.0150
5403	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.3744	0.0004	0.0003
7579	Acidobacteria	Acidobacteria	Acidobacteriales	Acidobacteriaceae	unclassified	1.3715	0.0016	0.0009
2230	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Morganella	1.3715	0.0221	0.0077

8037	Proteobacteria	Alphaproteobacteria	Rhodospirillales	Rhodospirillaceae	Phaeospirillum	1.3651	0.0096	0.0039
6115	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	1.3646	0.0456	0.0143
5666	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	1.3634	0.0038	0.0018
10181	Cyanobacteria	Chloroplast	Euglenozoa	unclassified	sfD	1.3590	0.0000	0.0000
1366	BRC1	PRR-11	unclassified	unclassified	sfA	1.3551	0.0034	0.0016
7068	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.3535	0.0151	0.0057
4763	Proteobacteria	Betaproteobacteria	Burkholderiales	Oxalobacteraceae	unclassified	1.3531	0.0446	0.0141
945	Actinobacteria	Actinobacteria	Actinomycetales	Streptomycetaceae	unclassified	1.3464	0.0140	0.0054
6413	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.3422	0.0041	0.0019
8714	Bacteroidetes	Bacteroidia	Bacteroidales	RikenellaceaeII	unclassified	1.3393	0.0138	0.0053
10686	CD12	MB-B2-116	unclassified	unclassified	sfB	1.3349	0.0018	0.0010
4998	Proteobacteria	Betaproteobacteria	Burkholderiales	Burkholderiaceae	Cupriavidus	1.3346	0.0000	0.0000
4083	Proteobacteria	Betaproteobacteria	Burkholderiales	Burkholderiaceae	Ralstonia	1.3293	0.0123	0.0049
604	Actinobacteria	Actinobacteria	Actinomycetales	Streptomycetaceae	Streptomyces	1.3249	0.0006	0.0004
10140	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	1.3228	0.0000	0.0000
5480	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.3175	0.0036	0.0017
6491	Spirochaetes	Spirochaetes	Spirochaetales	Spirochaetaceae	unclassified	1.3119	0.0040	0.0019
5733	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.3110	0.0006	0.0004
6515	Firmicutes	Bacilli	Bacillales	Bacillaceae	Geobacillus	1.3030	0.0155	0.0058
3376	Chloroflexi	Dehalococcoidetes	Dehalococcoidales	Dehalococcoidaceae	unclassified	1.2917	0.0242	0.0083
6264	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.2897	0.0041	0.0019
5772	Firmicutes	Bacilli	Bacillales	Paenibacillaceae	Paenibacillus	1.2881	0.0362	0.0118
5774	Proteobacteria	Epsilonproteobacteria	Campylobacterales	Helicobacteraceae	Sulfurovum	1.2814	0.0231	0.0079
5220	Proteobacteria	Gammaproteobacteria	Alteromonadales	Pseudoalteromonadaceae	Pseudoalteromonas	1.2813	0.0082	0.0034
7112	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	1.2751	0.0024	0.0013
5353	Verrucomicrobia	Verrucomicrobiae	Verrucomicrobiales	Verrucomicrobia subdivision 3	unclassified	1.2747	0.0006	0.0004
7953	Bacteroidetes	Bacteroidia	Bacteroidales	RikenellaceaeII	unclassified	1.2746	0.0079	0.0033
3694	Thermi	Deinococci	Deinococcales	Deinococcaceae	Deinococcus	1.2736	0.0019	0.0010
7269	Bacteroidetes	Bacteroidia	Bacteroidales	RikenellaceaeII	unclassified	1.2709	0.0282	0.0095
5276	Proteobacteria	Gammaproteobacteria	Alteromonadales	Alteromonadaceae	Alteromonas	1.2698	0.0126	0.0049
7872	Proteobacteria	Deltaproteobacteria	Desulfovibrionales	Desulfovibrionaceae	unclassified	1.2681	0.0030	0.0015
8206	Bacteroidetes	Bacteroidia	Bacteroidales	RikenellaceaeII	unclassified	1.2651	0.0485	0.0150
9784	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	1.2613	0.0007	0.0005
3860	Spirochaetes	WWE1	PBS-18	SHA-4	W22	1.2572	0.0114	0.0045
8171	Bacteroidetes	Bacteroidia	Bacteroidales	RikenellaceaeII	unclassified	1.2553	0.0033	0.0016
3516	Proteobacteria	Gammaproteobacteria	Xanthomonadales	Xanthomonadaceae	Stenotrophomonas	1.2539	0.0071	0.0030
8235	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	1.2528	0.0067	0.0029
9783	Firmicutes	Clostridia	Clostridiales	Clostridiales Family XIII. Incertae Sedis	Eubacterium	1.2473	0.0000	0.0000
9162	Proteobacteria	Deltaproteobacteria	Entotheonellales	Entotheonellaceae	Candidatus Entotheonella	1.2406	0.0202	0.0072
10731	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Faecalibacterium	1.2393	0.0440	0.0140
8726	Bacteroidetes	Bacteroidia	Bacteroidales	Porphyromonadaceae	Dysgonomonas	1.2373	0.0330	0.0109
7413	Bacteroidetes	Bacteroidia	Bacteroidales	Porphyromonadaceae	unclassified	1.2356	0.0012	0.0008
7071	Spirochaetes	Spirochaetes	Spirochaetales	Spirochaetaceae	Treponema	1.2346	0.0003	0.0002
8685	Cyanobacteria	Nostocophycideae	Nostocales	Nostocaceae	Trichormus	1.2312	0.0013	0.0008
8028	Bacteroidetes	Bacteroidia	Bacteroidales	RikenellaceaeII	unclassified	1.2285	0.0194	0.0069
1146	Actinobacteria	Actinobacteria	Bifidobacteriales	Bifidobacteriaceae	Bifidobacterium	1.2279	0.0230	0.0079
6586	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	1.2262	0.0443	0.0140
4013	Proteobacteria	Betaproteobacteria	Burkholderiales	Burkholderiaceae	Ralstonia	1.2191	0.0160	0.0059
4684	Proteobacteria	Betaproteobacteria	Burkholderiales	Alcaligenaceae	Achromobacter	1.2157	0.0174	0.0064
1368	Actinobacteria	Actinobacteria	Actinomycetales	Streptomycetaceae	Streptomyces	1.1912	0.0299	0.0099
5645	Spirochaetes	Spirochaetes	Spirochaetales	Spirochaetaceae	Treponema	1.1841	0.0197	0.0070
9708	Firmicutes	Clostridia	Clostridiales	Catabacteriaceae	unclassified	1.1768	0.0455	0.0143
1054	Candidatus Poribacteria	unclassified	unclassified	unclassified	sfA	1.1717	0.0099	0.0040
9608	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	1.1676	0.0414	0.0133
6365	Firmicutes	Bacilli	Lactobacillales	Enterococcaceae	Enterococcus	1.1659	0.0227	0.0078
8955	Bacteroidetes	Bacteroidia	Bacteroidales	RikenellaceaeII	unclassified	1.1472	0.0382	0.0124
9516	Tenericutes	Mollicutes	Entomoplasmatales	Spiroplasmataceae	Spiroplasma	1.1049	0.0497	0.0153
3488	Proteobacteria	Gammaproteobacteria	Thiotrichales	Thiotrichaceae	unclassified	0.8782	0.0427	0.0137
208	Actinobacteria	Actinobacteria	Actinomycetales	Streptomycetaceae	Streptomyces	0.8378	0.0296	0.0098
8473	Bacteroidetes	Bacteroidia	Bacteroidales	RikenellaceaeII	unclassified	0.8291	0.0042	0.0019
8241	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	unclassified	0.8026	0.0209	0.0074
4482	Spirochaetes	WWE1	PBS-18	SHA-116	unclassified	0.7875	0.0158	0.0059
10861	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.7823	0.0078	0.0033
340	VHS-B3-43	unclassified	unclassified	unclassified	sfA	0.7802	0.0258	0.0088
8403	Cyanobacteria	Nostocophycideae	Nostocales	Nostocaceae	Dolichospermum	0.7792	0.0184	0.0067
2880	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	0.7790	0.0378	0.0123
9865	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.7788	0.0031	0.0015
4556	Proteobacteria	Betaproteobacteria	Burkholderiales	Oxalobacteraceae	Oxalobacter	0.7748	0.0024	0.0013
9170	Bacteroidetes	Bacteroidia	Bacteroidales	RikenellaceaeII	unclassified	0.7650	0.0196	0.0070
5088	Proteobacteria	Gammaproteobacteria	Xanthomonadales	Xanthomonadaceae	Stenotrophomonas	0.7505	0.0087	0.0036
1575	Actinobacteria	Actinobacteria	Actinomycetales	Streptomycetaceae	Streptomyces	0.7499	0.0354	0.0116
9314	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Ruminococcus	0.7483	0.0433	0.0138
10559	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	0.7361	0.0008	0.0006
245	WS3	PRR-12	unclassified	unclassified	sfA	0.7332	0.0189	0.0068
337	Actinobacteria	Actinobacteria	Actinomycetales	Micromonosporaceae	Micromonospora	0.7201	0.0139	0.0053
1230	Actinobacteria	Actinobacteria	Actinomycetales	Streptomycetaceae	Streptomyces	0.7040	0.0068	0.0029
9395	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.7017	0.0017	0.0009
10858	MSBL6	EubG1	unclassified	unclassified	sfA	0.6916	0.0002	0.0002
7324	Acidobacteria	Acidobacteria	Acidobacteriales	Acidobacteriaceae	unclassified	0.6906	0.0001	0.0001
1265	Actinobacteria	Actinobacteria	Actinomycetales	Streptomycetaceae	Streptomyces	0.6900	0.0018	0.0010
3684	Fibrobacteres	Fibrobacteres	Fibrobacterales	Fibrobacteraceae	Fibrobacter	0.6890	0.0013	0.0008
406	Actinobacteria	Actinobacteria	Actinomycetales	Streptomycetaceae	Streptomyces	0.6859	0.0104	0.0042
5886	Spirochaetes	Spirochaetes	Spirochaetales	Spirochaetaceae	Treponema	0.6846	0.0002	0.0001
9760	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Clostridium	0.6795	0.0003	0.0002
6119	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.6777	0.0137	0.0053
9585	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	0.6776	0.0000	0.0000
9901	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.6743	0.0009	0.0006
8996	Bacteroidetes	Flavobacteria	Flavobacteriales	Cryomorphaceae	unclassified	0.6738	0.0212	0.0074
431	Planctomycetes	Phycisphaerae	Phycisphaerales	unclassified	sfB	0.6655	0.0080	0.0033

10327	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	0.6475	0.0000	0.0000
7148	Bacteroidetes	Bacteroidia	Bacteroidales	Rikenellaceae	Alistipes	0.6391	0.0012	0.0008
10952	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Coprococcus	0.6314	0.0001	0.0001
7194	Proteobacteria	Deltaproteobacteria	Desulfovibrionales	Desulfovibrionaceae	Desulfovibrio	0.6292	0.0001	0.0001
10786	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	0.6291	0.0432	0.0138
9020	Bacteroidetes	Bacteroidia	Bacteroidales	RikenellaceaeII	unclassified	0.6242	0.0003	0.0002
11011	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Shuttleworthia	0.6181	0.0115	0.0045
9204	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Blautia	0.6147	0.0124	0.0049
9203	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.6129	0.0482	0.0150
4185	Synergistetes	Synergistia	Synergistales	Dethiosulfovibrionaceae	Pyramidobacter	0.6122	0.0181	0.0066
10536	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.6059	0.0004	0.0003
10705	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Butyrivibrio	0.6057	0.0062	0.0027
7347	Cyanobacteria	Nostocophycideae	Nostocales	Nostocaceae	Dolichospermum	0.6019	0.0000	0.0000
10892	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.5946	0.0186	0.0067
9746	Firmicutes	Clostridia	Clostridiales	Clostridiales Family XIII. Incertae Sedis	Eubacterium	0.5925	0.0015	0.0009
9620	Thermotogae	Thermotogae	Thermotogales	Thermotogaceae	Kosmotoga	0.5878	0.0002	0.0002
4553	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.5873	0.0021	0.0011
8956	Proteobacteria	Deltaproteobacteria	Desulfovibrionales	Desulfovibrionaceae	Desulfovibrio	0.5863	0.0016	0.0009
8166	Cyanobacteria	Nostocophycideae	Nostocales	Nostocaceae	Dolichospermum	0.5619	0.0000	0.0000
8804	Cyanobacteria	Nostocophycideae	Nostocales	Nostocaceae	Dolichospermum	0.5454	0.0000	0.0000
11079	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Coprococcus	0.5438	0.0000	0.0000
3546	Proteobacteria	Deltaproteobacteria	Desulfobacterales	Nitrospinaceae	unclassified	0.5431	0.0002	0.0001
9810	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.5383	0.0050	0.0022
1824	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	0.5345	0.0065	0.0028
10665	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.5332	0.0000	0.0000
4705	Proteobacteria	Gammaproteobacteria	Chromatiales	Ectothiorhodospiraceae	unclassified	0.5332	0.0001	0.0001
10931	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.5234	0.0006	0.0004
10986	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.5044	0.0000	0.0000
240	Actinobacteria	Actinobacteria	Actinomycetales	Streptomycetaceae	Streptomyces	0.4987	0.0046	0.0021
10768	Proteobacteria	Alphaproteobacteria	Rhizobiales	Bradyrhizobiaceae	Bradyrhizobium	0.4949	0.0028	0.0014
5016	Proteobacteria	Betaproteobacteria	Burkholderiales	Burkholderiaceae	Ralstonia	0.4842	0.0004	0.0003
10828	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.4756	0.0001	0.0001
6043	Acidobacteria	Chloracidobacteria	unclassified	unclassified	sfA	0.4675	0.0003	0.0002
7452	Actinobacteria	Actinobacteria	Solirubrobacterales	Conexibacteraceae	unclassified	0.4654	0.0000	0.0000
11066	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Lachnobacterium	0.4631	0.0000	0.0000
8954	Cyanobacteria	Nostocophycideae	Nostocales	Nostocaceae	Dolichospermum	0.4502	0.0016	0.0009
3884	Firmicutes	Clostridia	Clostridiales	Syntrophomonadaceae	Syntrophomonas	0.4479	0.0295	0.0098
396	Actinobacteria	Actinobacteria	Bifidobacteriales	Bifidobacteriaceae	Bifidobacterium	0.4436	0.0016	0.0009
2903	Proteobacteria	Gammaproteobacteria	Vibrionales	Vibrionaceae	Vibrio	0.4434	0.0001	0.0001
11058	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Clostridium	0.4383	0.0000	0.0000
10508	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	0.4270	0.0000	0.0000
4744	Firmicutes	Clostridia	Clostridiales	Syntrophomonadaceae	Syntrophomonas	0.4215	0.0019	0.0010
7461	Proteobacteria	Alphaproteobacteria	Sphingomonadales	Erythrobacteraceae	unclassified	0.4150	0.0010	0.0006
9745	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.4024	0.0003	0.0002
8002	Cyanobacteria	Nostocophycideae	Nostocales	Nostocaceae	Dolichospermum	0.3941	0.0002	0.0002
10436	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	0.3920	0.0069	0.0030
7713	Cyanobacteria	Nostocophycideae	Nostocales	Nostocaceae	Dolichospermum	0.3901	0.0000	0.0000
9719	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.3820	0.0000	0.0000
6679	Acidobacteria	Acidobacteria	Acidobacteriales	Acidobacteriaceae	unclassified	0.3804	0.0000	0.0000
7636	Cyanobacteria	Nostocophycideae	Nostocales	Nostocaceae	Dolichospermum	0.3782	0.0000	0.0000
9804	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Anaerotruncus	0.3757	0.0003	0.0003
4975	Deferribacteres	Deferribacteres	Deferribacterales	Calithrixaceae	Caldithrix	0.3753	0.0019	0.0010
2149	Bacteroidetes	Sphingobacteria	Sphingobacteriales	Flammeovirgaceae	unclassified	0.3546	0.0000	0.0000
9196	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Faecalibacterium	0.3418	0.0000	0.0000
9166	Acidobacteria	Sva0725	Sva0725	unclassified	sfE	0.3316	0.0000	0.0000
9186	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.3299	0.0000	0.0000
7730	Proteobacteria	Deltaproteobacteria	Desulfovibrionales	Desulfohalobiaceae	Desulfonauticus	0.3286	0.0002	0.0002
7616	Cyanobacteria	Oscillatoriophycideae	Chroococcales	Spirulinaceae	Spirulina	0.3226	0.0000	0.0000
9442	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.3176	0.0002	0.0002
2004	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Yersinia	0.3147	0.0004	0.0003
7787	Proteobacteria	Deltaproteobacteria	Myxococcales	Haliangiaceae	unclassified	0.3041	0.0033	0.0016
7722	Bacteroidetes	Bacteroidia	Bacteroidales	Porphyromonadaceae	unclassified	0.3013	0.0000	0.0000
9757	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Clostridium	0.2966	0.0001	0.0001
10788	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Butyrivibrio	0.2956	0.0000	0.0000
10430	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Clostridium	0.2920	0.0000	0.0000
11024	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	0.2904	0.0002	0.0002
10844	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	0.2893	0.0001	0.0001
10709	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Butyrivibrio	0.2843	0.0000	0.0000
5204	GOUTA4	RB384	unclassified	unclassified	sfA	0.2822	0.0000	0.0000
9705	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.2800	0.0047	0.0021
10471	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Clostridium	0.2788	0.0000	0.0000
9451	Proteobacteria	Alphaproteobacteria	Rhizobiales	Hyphomicrobiaceae	Rhodoplanes	0.2723	0.0000	0.0000
8314	Cyanobacteria	Oscillatoriophycideae	Oscillatoriales	unclassified	sfA	0.2723	0.0016	0.0009
9294	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	0.2663	0.0000	0.0000
9676	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Coprococcus	0.2629	0.0000	0.0000
10025	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Clostridium	0.2559	0.0000	0.0000
10409	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Lachnospira	0.2498	0.0000	0.0000
10493	Firmicutes	Clostridia	Clostridiales	Clostridiales Family XI. Incertae Sedis	Peptoniphilus	0.2492	0.0000	0.0000
5497	Proteobacteria	Epsilonproteobacteria	Campylobacterales	Campylobacteraceae	Campylobacter	0.2447	0.0000	0.0000
10664	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.2413	0.0000	0.0000
6797	Acidobacteria	RB25	unclassified	unclassified	sfA	0.2306	0.0000	0.0000
2558	Proteobacteria	Gammaproteobacteria	Oceanospirillales	OM60	unclassified	0.2299	0.0127	0.0049
10341	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Ruminococcus	0.2255	0.0000	0.0000
11092	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Dorea	0.2105	0.0016	0.0009
8788	Proteobacteria	Alphaproteobacteria	Rhodospirillales	Rhodospirillaceae	Tistrella	0.2089	0.0000	0.0000
9478	Proteobacteria	Alphaproteobacteria	Rhizobiales	Hyphomicrobiaceae	Hyphomicrobium	0.2030	0.0000	0.0000
9594	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.2024	0.0004	0.0003
2829	Proteobacteria	Gammaproteobacteria	Alteromonadales	Shewanellaceae	Shewanella	0.2017	0.0006	0.0004
11084	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Coprococcus	0.1984	0.0000	0.0000

3648	Proteobacteria	Gammaproteobacteria	Legionellales	Legionellaceae	unclassified	0.1863	0.0000	0.0000
10032	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Clostridium	0.1758	0.0000	0.0000
9843	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Blautia	0.1566	0.0003	0.0002
2105	Proteobacteria	Gammaproteobacteria	Aeromonadales	Aeromonadaceae	Aeromonas	0.1553	0.0000	0.0000
9556	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Blautia	0.1540	0.0000	0.0000
9913	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	Clostridium	0.1430	0.0000	0.0000
10132	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	0.1217	0.0000	0.0000
10435	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Coprococcus	0.1201	0.0000	0.0000
1965	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Yersinia	0.1000	0.0001	0.0001
6811	Proteobacteria	Epsilonproteobacteria	Campylobacterales	Helicobacteraceae	Sulfurovum	0.0969	0.0000	0.0000
9866	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.0965	0.0000	0.0000
10654	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Ruminococcus	0.0962	0.0000	0.0000
10500	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Eubacterium	0.0888	0.0000	0.0000
10842	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.0885	0.0000	0.0000
9828	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Roseburia	0.0872	0.0000	0.0000
11125	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	0.0492	0.0000	0.0000
7845	Bacteroidetes	Bacteroidia	Bacteroidales	Porphyromonadaceae	Parabacteroides	0.0465	0.0000	0.0000
11017	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Bacteroides	0.0252	0.0000	0.0000
10303	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	0.0224	0.0000	0.0000

Table S2. Significantly enriched bacterial OTUs - Control Ileum vs. Control Cecum. Table sorted by Fold Change. T-test p-value < 0.05, q-value < 0.12

OTU	Phylum	Class	Order	Family	Genus	Fold Change (Ileum / Cecum)	pvalue	qvalue
6543	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	4.7807	0.0001	0.0000
6139	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	4.2112	0.0062	0.0018
6711	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	3.7150	0.0000	0.0000
6515	Firmicutes	Bacilli	Bacillales	Bacillaceae	Geobacillus	3.5641	0.0004	0.0002
5628	Firmicutes	Bacilli	Bacillales	Paenibacillaceae	Paenibacillus	3.3853	0.0000	0.0000
8942	Proteobacteria	Alphaproteobacteria	Rhodospirillales	Acetobacteraceae	Asaia	3.0306	0.0000	0.0000
6568	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	2.9878	0.0000	0.0000
6478	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	2.8935	0.0000	0.0000
6003	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	2.8631	0.0000	0.0000
5620	Firmicutes	Bacilli	Bacillales	Bacillaceae	unclassified	2.8095	0.0000	0.0000
6646	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	2.8004	0.0000	0.0000
6233	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	2.7546	0.0000	0.0000
5730	Spirochaetes	Spirochaetes	Spirochaetales	Spirochaetaceae	IE043	2.7224	0.0000	0.0000
5946	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	2.6468	0.0002	0.0001
6107	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	2.5872	0.0000	0.0000
6913	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	2.5715	0.0000	0.0000
2747	Proteobacteria	Gammaproteobacteria	Oceanospirillales	ZA3412c	unclassified	2.5690	0.0000	0.0000
6624	Firmicutes	Bacilli	Turicibacterales	Turicibacteraceae	Turicibacter	2.4756	0.0000	0.0000
6599	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	2.4735	0.0000	0.0000
6923	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	2.4710	0.0000	0.0000
5835	Firmicutes	Bacilli	Bacillales	Paenibacillaceae	Paenibacillus	2.4414	0.0000	0.0000
6502	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	2.4147	0.0002	0.0001
9993	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	2.3893	0.0000	0.0000
5947	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	2.3091	0.0001	0.0001
6387	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	2.2681	0.0003	0.0001
7579	Acidobacteria	Acidobacteria	Acidobacteriales	Acidobacteriaceae	unclassified	2.2681	0.0000	0.0000
6402	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	2.2546	0.0002	0.0001
5791	Firmicutes	Bacilli	Bacillales	Bacillaceae	Salinibacillus	2.2153	0.0000	0.0000
5829	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	2.2029	0.0000	0.0000
6068	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	2.1959	0.0000	0.0000
10836	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	Clostridium	2.1862	0.0000	0.0000
9826	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	Clostridium	2.1524	0.0001	0.0000
6488	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	2.1331	0.0000	0.0000
6900	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	2.1243	0.0030	0.0009
5839	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	2.1100	0.0000	0.0000
8147	Proteobacteria	Deltaproteobacteria	Syntrophobacterales	Desulfobacteraceae	Desulfococcus	2.1099	0.0000	0.0000
6544	Firmicutes	Bacilli	Bacillales	Planococcaceae	Planomicrobium	2.0739	0.0000	0.0000
4083	Proteobacteria	Betaproteobacteria	Burkholderiales	Burkholderiaceae	Ralstonia	2.0487	0.0003	0.0001
6379	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	2.0469	0.0000	0.0000
6115	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	2.0441	0.0001	0.0000
6572	Firmicutes	Bacilli	Bacillales	Bacillaceae	Geobacillus	2.0296	0.0000	0.0000
5428	Firmicutes	Bacilli	Bacillales	Paenibacillaceae	Paenibacillus	2.0222	0.0000	0.0000
6726	Firmicutes	Bacilli	Bacillales	Bacillaceae	Geobacillus	2.0120	0.0000	0.0000
5046	Verrucomicrobia	Verrucomicrobiae	Verrucomicrobiales	unclassified	sfH	2.0014	0.0000	0.0000
1243	Actinobacteria	Actinobacteria	Actinomycetales	Streptomycetaceae	Streptomyces	1.9973	0.0000	0.0000
7080	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.9911	0.0001	0.0000
6959	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.9865	0.0000	0.0000
11099	Tenericutes	Erysipelotrichi	Erysipelotrichales	Erysipelotrichaceae	PSB-M-3	1.9679	0.0000	0.0000
9995	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Ruminococcus	1.9324	0.0001	0.0000
9655	Tenericutes	Mollicutes	Acholeplasmatales	Acholeplasmataceae	Candidatus Phytoplasma	1.9087	0.0002	0.0001
10989	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	Clostridium	1.8760	0.0001	0.0001
9783	Firmicutes	Clostridia	Clostridiales	Clostridiales Family XIII. Incertae Sedis	Eubacterium	1.8469	0.0001	0.0000
1041	AD3	ABS-6	unclassified	unclassified	sfA	1.8288	0.0000	0.0000
5961	Firmicutes	Bacilli	Bacillales	Bacillaceae	Geobacillus	1.8271	0.0000	0.0000

6235	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.8245	0.0000	0.0000
7112	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	1.7996	0.0000	0.0000
5857	Firmicutes	Bacilli	Bacillales	Bacillaceae	Geobacillus	1.7892	0.0000	0.0000
8685	Cyanobacteria	Nostocophycideae	Nostocales	Nostocaceae	Trichormus	1.7866	0.0000	0.0000
5629	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.7578	0.0000	0.0000
7136	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Pediococcus	1.7459	0.0012	0.0004
3814	Firmicutes	Clostridia	MBA08	unclassified	sfA	1.7440	0.0000	0.0000
5276	Proteobacteria	Gammaproteobacteria	Alteromonadales	Alteromonadaceae	Alteromonas	1.7389	0.0001	0.0000
88	Actinobacteria	Actinobacteria	Bifidobacteriales	Bifidobacteriaceae	Bifidobacterium	1.7262	0.0000	0.0000
10012	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	1.7225	0.0040	0.0012
6997	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.7141	0.0000	0.0000
5401	Firmicutes	Bacilli	Bacillales	Paenibacillaceae	Paenibacillus	1.7097	0.0000	0.0000
5666	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	1.7050	0.0000	0.0000
6583	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.6832	0.0000	0.0000
5842	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.6822	0.0000	0.0000
2203	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	1.6810	0.0002	0.0001
5524	Firmicutes	Bacilli	Bacillales	Alicyclobacillaceae	Alicyclobacillus	1.6625	0.0004	0.0002
6633	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.6588	0.0000	0.0000
7300	Proteobacteria	Alphaproteobacteria	Rhodospirillales	Rhodospirillaceae	unclassified	1.6555	0.0000	0.0000
8246	Bacteroidetes	Bacteroidia	Bacteroidales	RikenellaceaeII	unclassified	1.6331	0.0000	0.0000
8114	Proteobacteria	Alphaproteobacteria	Rhodospirillales	Rhodospirillaceae	unclassified	1.6270	0.0008	0.0003
4990	Verrucomicrobia	Verrucomicrobiae	Verrucomicrobiales	Verrucomicrobiaceae	Akkermansia	1.6232	0.0023	0.0007
6947	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.6089	0.0000	0.0000
1366	BRC1	PRR-11	unclassified	unclassified	sfA	1.5902	0.0010	0.0004
9683	Caldiserica	OP5	LF045	062DZ04	unclassified	1.5833	0.0485	0.0116
5389	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.5636	0.0000	0.0000
7548	Bacteroidetes	Bacteroidia	Bacteroidales	Porphyromonadaceae	unclassified	1.5380	0.0003	0.0001
6042	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.5360	0.0000	0.0000
7071	Spirochaetes	Spirochaetes	Spirochaetales	Spirochaetaceae	Treponema	1.5346	0.0000	0.0000
7068	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.5276	0.0008	0.0003
10877	Cyanobacteria	Chloroplast	Streptophyta	unclassified	sfA	1.5148	0.0000	0.0000
9724	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	Clostridium	1.5062	0.0285	0.0073
4763	Proteobacteria	Betaproteobacteria	Burkholderiales	Oxalobacteraceae	unclassified	1.5014	0.0097	0.0027
467	Lentisphaerae	Lentisphaerae	Victivallales	Victivallaceae	unclassified	1.4965	0.0013	0.0004
2833	Proteobacteria	Gammaproteobacteria	Vibrionales	Vibrionaceae	Vibrio	1.4964	0.0110	0.0031
5403	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.4693	0.0000	0.0000
5684	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.4680	0.0013	0.0004
1914	Bacteroidetes	Sphingobacteria	Sphingobacteriales	Flammeovirgaceae	Roseivirga	1.4638	0.0012	0.0004
6298	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.4613	0.0001	0.0000
5676	Spirochaetes	Spirochaetes	Spirochaetales	Spirochaetaceae	Treponema	1.4579	0.0117	0.0032
10686	CD12	MB-B2-116	unclassified	unclassified	sfB	1.4572	0.0000	0.0000
6169	Acidobacteria	Chloracidobacteria	unclassified	unclassified	sfA	1.4563	0.0447	0.0109
10181	Cyanobacteria	Chloroplast	Euglenozoa	unclassified	sfD	1.4550	0.0000	0.0000
6413	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.4440	0.0001	0.0000
5772	Firmicutes	Bacilli	Bacillales	Paenibacillaceae	Paenibacillus	1.4415	0.0041	0.0012
8714	Bacteroidetes	Bacteroidia	Bacteroidales	RikenellaceaeII	unclassified	1.4361	0.0010	0.0003
5444	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.4349	0.0000	0.0000
4910	Proteobacteria	Gammaproteobacteria	Pseudomonadales	Moraxellaceae	Moraxella	1.4252	0.0094	0.0027
9162	Proteobacteria	Deltaproteobacteria	Entotheonellales	Entotheonellaceae	Candidatus Entotheonella	1.4239	0.0000	0.0000
6586	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	1.4222	0.0000	0.0000
6229	Spirochaetes	Spirochaetes	Spirochaetales	Spirochaetaceae	Treponema	1.4214	0.0000	0.0000
9516	Tenericutes	Mollicutes	Entomoplasmatales	Spiroplasmataceae	Spiroplasma	1.4205	0.0000	0.0000
6365	Firmicutes	Bacilli	Lactobacillales	Enterococcaceae	Enterococcus	1.4134	0.0008	0.0003
10731	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Faecalibacterium	1.4126	0.0040	0.0012
1239	Actinobacteria	Actinobacteria	Actinomycetales	Intrasporangiaceae	Knoellia	1.4066	0.0013	0.0004
5817	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.4065	0.0000	0.0000
10204	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Ruminococcus	1.4059	0.0147	0.0040
4057	Deferribacteres	Deferribacteres	Deferribacterales	Calithrixaceae	Caldithrix	1.3989	0.0041	0.0012
6408	Firmicutes	Bacilli	Bacillales	Alicyclobacillaceae	Alicyclobacillus	1.3893	0.0010	0.0004
5645	Spirochaetes	Spirochaetes	Spirochaetales	Spirochaetaceae	Treponema	1.3883	0.0000	0.0000
5353	Verrucomicrobia	Verrucomicrobiae	Verrucomicrobiales	Verrucomicrobia subdivision 3	unclassified	1.3828	0.0000	0.0000
9918	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	1.3650	0.0001	0.0000
781	Elusimicrobia	Elusimicrobia	Elusimicrobiales	unclassified	sfA	1.3516	0.0118	0.0033
4749	Deferribacteres	Deferribacteres	Deferribacterales	Calithrixaceae	Caldithrix	1.3475	0.0059	0.0018
7790	Bacteroidetes	Flavobacteria	Flavobacteriales	Flavobacteriaceae	unclassified	1.3461	0.0182	0.0049
5733	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.3433	0.0002	0.0001
10599	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Clostridium	1.3360	0.0000	0.0000
5642	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.3147	0.0269	0.0070
8037	Proteobacteria	Alphaproteobacteria	Rhodospirillales	Rhodospirillaceae	Phaeospirillum	1.3022	0.0229	0.0060
4998	Proteobacteria	Betaproteobacteria	Burkholderiales	Burkholderiaceae	Cupriavidus	1.2980	0.0001	0.0000
2574	Bacteroidetes	Sphingobacteria	Sphingobacteriales	Flammeovirgaceae	unclassified	1.2806	0.0398	0.0098
4380	Proteobacteria	Betaproteobacteria	Burkholderiales	Burkholderiaceae	Ralstonia	1.2795	0.0000	0.0000
6264	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.2741	0.0030	0.0009
5803	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.2710	0.0225	0.0059
5480	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.2649	0.0003	0.0001
604	Actinobacteria	Actinobacteria	Actinomycetales	Streptomycetaceae	Streptomyces	1.2601	0.0012	0.0004
3509	Firmicutes	Clostridia	Thermoanaerobacterales	Thermoanaerobacteraceae	unclassified	1.2579	0.0007	0.0002
10572	Proteobacteria	Alphaproteobacteria	Rhodospirillales	Rhodospirillaceae	unclassified	1.2546	0.0128	0.0035
10140	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	1.2438	0.0008	0.0003
8726	Bacteroidetes	Bacteroidia	Bacteroidales	Porphyromonadaceae	Dysgonomonas	1.2390	0.0224	0.0059
3516	Proteobacteria	Gammaproteobacteria	Xanthomonadales	Xanthomonadaceae	Stenotrophomonas	1.2348	0.0021	0.0007
10938	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	1.2287	0.0061	0.0018
7872	Proteobacteria	Deltaproteobacteria	Desulfovibrionales	Desulfovibrionaceae	unclassified	1.2282	0.0010	0.0003
6491	Spirochaetes	Spirochaetes	Spirochaetales	Spirochaetaceae	unclassified	1.2188	0.0137	0.0038
1368	Actinobacteria	Actinobacteria	Actinomycetales	Streptomycetaceae	Streptomyces	1.2134	0.0087	0.0025
8086	Proteobacteria	Alphaproteobacteria	Caulobacterales	Caulobacteraceae	Brevundimonas	1.2103	0.0124	0.0034
8171	Bacteroidetes	Bacteroidia	Bacteroidales	RikenellaceaeII	unclassified	1.2076	0.0223	0.0059
9579	Tenericutes	Erysipelotrichi	Erysipelotrichales	Erysipelotrichaceae	Pei061	1.2016	0.0011	0.0004
7575	Proteobacteria	Alphaproteobacteria	Rhizobiales	Nordellaceae	Nordella	1.2009	0.0012	0.0004

3334	Proteobacteria	Gammaproteobacteria	Pseudomonadales	Pseudomonadaceae	Pseudomonas	1.1968	0.0188	0.0050
8866	Bacteroidetes	Bacteroidia	Bacteroidales	Porphyromonadaceae	unclassified	1.1931	0.0449	0.0109
7953	Bacteroidetes	Bacteroidia	Bacteroidales	RikenellaceaeII	unclassified	1.1635	0.0397	0.0098
3694	Thermi	Deinococci	Deinococcales	Deinococcaceae	Deinococcus	1.1483	0.0335	0.0084
678	Actinobacteria	Actinobacteria	Actinomycetales	Corynebacteriaceae	Corynebacterium	1.1389	0.0337	0.0084
7413	Bacteroidetes	Bacteroidia	Bacteroidales	Porphyromonadaceae	unclassified	1.1234	0.0410	0.0101
1478	Actinobacteria	Actinobacteria	Actinomycetales	Streptomycetaceae	Streptomyces	0.9080	0.0325	0.0082
6451	Acidobacteria	Solibacteres	Solibacterales	Solibacteraceae	Candidatus Solibacter	0.8901	0.0401	0.0099
7384	Bacteroidetes	Bacteroidia	Bacteroidales	RikenellaceaeII	unclassified	0.8582	0.0077	0.0022
9904	Proteobacteria	Alphaproteobacteria	Rickettsiales	Rickettsiaceae	Wolbachia	0.8557	0.0287	0.0073
8602	Proteobacteria	Deltaproteobacteria	Syntrophobacterales	Syntrophobacteraceae	unclassified	0.8487	0.0438	0.0107
10485	Tenericutes	Mollicutes	Entomoplasmatales	Spiroplasmataceae	Spiroplasma	0.8480	0.0417	0.0102
9489	Firmicutes	Clostridia	Clostridiales	Veillonellaceae	unclassified	0.8465	0.0480	0.0116
9697	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	0.8412	0.0267	0.0069
10895	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	Clostridium	0.8345	0.0348	0.0087
8283	Proteobacteria	Alphaproteobacteria	Rhodospirillales	Rhodospirillaceae	unclassified	0.8308	0.0087	0.0025
784	Actinobacteria	Actinobacteria	Actinomycetales	Streptomycetaceae	Streptomyces	0.8273	0.0191	0.0051
5698	Firmicutes	Bacilli	Bacillales	Thermoactinomycetaceae	Planifilum	0.8156	0.0209	0.0055
10256	Proteobacteria	Alphaproteobacteria	Rhizobiales	Bradyrhizobiaceae	Bradyrhizobium	0.8039	0.0002	0.0001
10540	Proteobacteria	Alphaproteobacteria	Rhizobiales	Bradyrhizobiaceae	Bradyrhizobium	0.7949	0.0002	0.0001
4618	Proteobacteria	Gammaproteobacteria	Pseudomonadales	Moraxellaceae	Acinetobacter	0.7845	0.0077	0.0022
6369	Proteobacteria	Epsilonproteobacteria	Campylobacterales	Helicobacteraceae	Helicobacter	0.7791	0.0016	0.0005
1345	Actinobacteria	Actinobacteria	Actinomycetales	Streptomycetaceae	Streptomyces	0.7782	0.0015	0.0005
1718	Lentisphaerae	Lentisphaerae	Lentisphaerales	Lentisphaeraceae	Lentisphaera	0.7769	0.0095	0.0027
11057	Cyanobacteria	Chloroplast	Streptophyta	unclassified	sfA	0.7678	0.0304	0.0077
10931	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.7489	0.0317	0.0080
10861	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.7467	0.0006	0.0002
4368	Spirochaetes	WWE1	PBS-18	SHA-4	W22	0.7418	0.0290	0.0074
7347	Cyanobacteria	Nostocophycideae	Nostocales	Nostocaceae	Dolichospermum	0.7388	0.0000	0.0000
9865	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.7379	0.0000	0.0000
340	VHS-B3-43	unclassified	unclassified	unclassified	sfA	0.7328	0.0106	0.0030
5088	Proteobacteria	Gammaproteobacteria	Xanthomonadales	Xanthomonadaceae	Stenotrophomonas	0.7308	0.0049	0.0015
8804	Cyanobacteria	Nostocophycideae	Nostocales	Nostocaceae	Dolichospermum	0.7301	0.0001	0.0001
8473	Bacteroidetes	Bacteroidia	Bacteroidales	RikenellaceaeII	unclassified	0.7288	0.0001	0.0000
2880	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	0.7259	0.0007	0.0002
9395	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.7188	0.0001	0.0000
10705	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Butyrivibrio	0.7175	0.0140	0.0038
8900	Nitrospirae	Nitrospira	Nitrospirales	FW	GOUTA7	0.7146	0.0025	0.0008
8996	Bacteroidetes	Flavobacteria	Flavobacteriales	Cryomorphaceae	unclassified	0.7083	0.0337	0.0084
10559	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	0.7083	0.0000	0.0000
1575	Actinobacteria	Actinobacteria	Actinomycetales	Streptomycetaceae	Streptomyces	0.7079	0.0182	0.0049
2169	AC1	LC-1	unclassified	unclassified	sfA	0.7060	0.0000	0.0000
9620	Thermotogae	Thermotogae	Thermotogales	Thermotogaceae	Kosmotoga	0.7035	0.0038	0.0012
8241	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	unclassified	0.7012	0.0028	0.0009
4482	Spirochaetes	WWE1	PBS-18	SHA-116	unclassified	0.6986	0.0017	0.0005
337	Actinobacteria	Actinobacteria	Actinomycetales	Micromonosporaceae	Micromonospora	0.6864	0.0043	0.0013
2611	Bacteroidetes	Sphingobacteria	Sphingobacteriales	Flexibacteraceae	unclassified	0.6863	0.0396	0.0098
8166	Cyanobacteria	Nostocophycideae	Nostocales	Nostocaceae	Dolichospermum	0.6855	0.0000	0.0000
6119	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.6849	0.0113	0.0032
406	Actinobacteria	Actinobacteria	Actinomycetales	Streptomycetaceae	Streptomyces	0.6841	0.0073	0.0021
10327	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	0.6840	0.0000	0.0000
709	Lentisphaerae	Lentisphaerae	Victivallales	Victivallaceae	unclassified	0.6718	0.0001	0.0000
4556	Proteobacteria	Betaproteobacteria	Burkholderiales	Oxalobacteraceae	Oxalobacter	0.6715	0.0000	0.0000
9314	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Ruminococcus	0.6715	0.0480	0.0116
10536	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.6711	0.0017	0.0005
10617	Proteobacteria	Alphaproteobacteria	Rhizobiales	Bradyrhizobiaceae	Bradyrhizobium	0.6688	0.0000	0.0000
7194	Proteobacteria	Deltaproteobacteria	Desulfovibrionales	Desulfovibrionaceae	Desulfovibrio	0.6668	0.0001	0.0001
2668	Chloroflexi	Anaerolineae	Anaerolineales	Anaerolinaceae	T78	0.6666	0.0274	0.0071
9020	Bacteroidetes	Bacteroidia	Bacteroidales	RikenellaceaeII	unclassified	0.6661	0.0010	0.0004
1265	Actinobacteria	Actinobacteria	Actinomycetales	Streptomycetaceae	Streptomyces	0.6629	0.0009	0.0003
431	Planctomycetes	Phycisphaerae	Phycisphaerales	unclassified	sfB	0.6428	0.0013	0.0004
5886	Spirochaetes	Spirochaetes	Spirochaetales	Spirochaetaceae	Treponema	0.6420	0.0000	0.0000
9204	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Blautia	0.6403	0.0148	0.0040
6614	Acidobacteria	Acidobacteria	Acidobacteriales	Acidobacteriaceae	unclassified	0.6307	0.0254	0.0066
9585	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	0.6307	0.0000	0.0000
9768	Proteobacteria	Alphaproteobacteria	Rhizobiales	Hyphomicrobiaceae	Hyphomicrobium	0.6216	0.0014	0.0005
1567	SPAM	0319-6G9	unclassified	unclassified	sfA	0.6208	0.0063	0.0018
6476	Acidobacteria	Solibacteres	Solibacterales	Solibacteraceae	Candidatus Solibacter	0.6192	0.0005	0.0002
8596	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	0.6166	0.0000	0.0000
1230	Actinobacteria	Actinobacteria	Actinomycetales	Streptomycetaceae	Streptomyces	0.6157	0.0003	0.0001
733	OP3	koll11	GIF10	unclassified	sfA	0.5999	0.0000	0.0000
1824	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	0.5974	0.0140	0.0038
9760	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Clostridium	0.5893	0.0000	0.0000
8707	Bacteroidetes	Sphingobacteria	Sphingobacteriales	Sphingobacteriaceae	unclassified	0.5843	0.0002	0.0001
10952	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Coprococcus	0.5706	0.0000	0.0000
9901	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.5670	0.0001	0.0000
9810	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.5621	0.0040	0.0012
1660	Chloroflexi	RA13C7	unclassified	unclassified	sfA	0.5581	0.0042	0.0013
3684	Fibrobacteres	Fibrobacteres	Fibrobacterales	Fibrobacteraceae	Fibrobacter	0.5421	0.0000	0.0000
10728	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Coprococcus	0.5406	0.0109	0.0031
5016	Proteobacteria	Betaproteobacteria	Burkholderiales	Burkholderiaceae	Ralstonia	0.5398	0.0001	0.0000
4185	Synergistetes	Synergistia	Synergistales	Dethiosulfovibrionaceae	Pyramidobacter	0.5311	0.0000	0.0000
4744	Firmicutes	Clostridia	Clostridiales	Syntrophomonadaceae	Syntrophomonas	0.5180	0.0008	0.0003
9746	Firmicutes	Clostridia	Clostridiales	Clostridiales Family XIII. Incertae Sedis	Eubacterium	0.5114	0.0003	0.0001
10858	MSBL6	EubG1	unclassified	unclassified	sfA	0.5075	0.0000	0.0000
10892	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.5021	0.0000	0.0000
7148	Bacteroidetes	Bacteroidia	Bacteroidales	Rikenellaceae	Alistipes	0.5018	0.0000	0.0000
6043	Acidobacteria	Chloracidobacteria	unclassified	unclassified	sfA	0.4996	0.0010	0.0003
11058	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Clostridium	0.4914	0.0001	0.0000

7324	Acidobacteria	Acidobacteria	Acidobacteriales	Acidobacteriaceae	unclassified	0.4900	0.0000	0.0000
10828	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.4880	0.0001	0.0000
240	Actinobacteria	Actinobacteria	Actinomycetales	Streptomycetaceae	Streptomyces	0.4791	0.0000	0.0000
10665	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.4770	0.0000	0.0000
8002	Cyanobacteria	Nostocophycideae	Nostocales	Nostocaceae	Dolichospermum	0.4757	0.0011	0.0004
10986	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.4594	0.0000	0.0000
8954	Cyanobacteria	Nostocophycideae	Nostocales	Nostocaceae	Dolichospermum	0.4573	0.0000	0.0000
4553	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.4504	0.0002	0.0001
10768	Proteobacteria	Alphaproteobacteria	Rhizobiales	Bradyrhizobiaceae	Bradyrhizobium	0.4377	0.0004	0.0002
11079	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Coprococcus	0.4299	0.0000	0.0000
7713	Cyanobacteria	Nostocophycideae	Nostocales	Nostocaceae	Dolichospermum	0.4258	0.0000	0.0000
10508	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	0.4106	0.0000	0.0000
7452	Actinobacteria	Actinobacteria	Solirubrobacterales	Conexibacteraceae	unclassified	0.4017	0.0000	0.0000
7801	Proteobacteria	Deltaproteobacteria	Desulfovibrionales	Desulfovibrionaceae	Desulfovibrio	0.4014	0.0040	0.0012
2558	Proteobacteria	Gammaproteobacteria	Oceanospirillales	OM60	unclassified	0.4008	0.0002	0.0001
10436	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	0.3973	0.0072	0.0021
9745	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.3932	0.0001	0.0000
2903	Proteobacteria	Gammaproteobacteria	Vibrionales	Vibrionaceae	Vibrio	0.3879	0.0000	0.0000
3546	Proteobacteria	Deltaproteobacteria	Desulfobacterales	Nitrospinaceae	unclassified	0.3859	0.0000	0.0000
396	Actinobacteria	Actinobacteria	Bifidobacteriales	Bifidobacteriaceae	Bifidobacterium	0.3850	0.0001	0.0000
8956	Proteobacteria	Deltaproteobacteria	Desulfovibrionales	Desulfovibrionaceae	Desulfovibrio	0.3844	0.0000	0.0000
7405	Proteobacteria	Alphaproteobacteria	Rhodospirillales	Rhodospirillaceae	unclassified	0.3841	0.0017	0.0005
3884	Firmicutes	Clostridia	Clostridiales	Syntrophomonadaceae	Syntrophomonas	0.3819	0.0199	0.0053
4705	Proteobacteria	Gammaproteobacteria	Chromatiales	Ectothiorhodospiraceae	unclassified	0.3775	0.0000	0.0000
11066	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Lachnobacterium	0.3719	0.0000	0.0000
2149	Bacteroidetes	Sphingobacteria	Sphingobacteriales	Flammeovirgaceae	unclassified	0.3656	0.0000	0.0000
7636	Cyanobacteria	Nostocophycideae	Nostocales	Nostocaceae	Dolichospermum	0.3554	0.0000	0.0000
10788	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Butyrivibrio	0.3475	0.0000	0.0000
9186	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.3378	0.0000	0.0000
9804	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Anaerotruncus	0.3333	0.0002	0.0001
6679	Acidobacteria	Acidobacteria	Acidobacteriales	Acidobacteriaceae	unclassified	0.3295	0.0000	0.0000
7461	Proteobacteria	Alphaproteobacteria	Sphingomonadales	Erythrobacteraceae	unclassified	0.3292	0.0000	0.0000
10709	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Butyrivibrio	0.3138	0.0000	0.0000
9719	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.3083	0.0000	0.0000
10430	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Clostridium	0.3075	0.0000	0.0000
8314	Cyanobacteria	Oscillatoriophycideae	Oscillatoriales	unclassified	sfA	0.3060	0.0009	0.0003
9676	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Coprococcus	0.2988	0.0000	0.0000
5311	Synergistetes	Synergistia	Synergistales	B6	E6	0.2971	0.0000	0.0000
5204	GOUTA4	RB384	unclassified	unclassified	sfA	0.2963	0.0000	0.0000
2004	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Yersinia	0.2956	0.0003	0.0001
9442	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.2784	0.0000	0.0000
11092	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Dorea	0.2770	0.0033	0.0010
9705	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.2764	0.0029	0.0009
7616	Cyanobacteria	Oscillatoriophycideae	Chroococcales	Spirulinaceae	Spirulina	0.2754	0.0000	0.0000
11024	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	0.2744	0.0000	0.0000
9757	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Clostridium	0.2739	0.0000	0.0000
9196	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Faecalibacterium	0.2717	0.0000	0.0000
4975	Deferribacteres	Deferribacteres	Deferribacterales	Calithrixaceae	Caldithrix	0.2570	0.0000	0.0000
10844	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	0.2551	0.0001	0.0000
9294	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	0.2529	0.0000	0.0000
8788	Proteobacteria	Alphaproteobacteria	Rhodospirillales	Rhodospirillaceae	Tistrella	0.2523	0.0000	0.0000
10471	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Clostridium	0.2399	0.0000	0.0000
7722	Bacteroidetes	Bacteroidia	Bacteroidales	Porphyromonadaceae	unclassified	0.2271	0.0000	0.0000
10493	Firmicutes	Clostridia	Clostridiales	Clostridiales Family XI. Incertae Sedis	Peptoniphilus	0.2191	0.0000	0.0000
9451	Proteobacteria	Alphaproteobacteria	Rhizobiales	Hyphomicrobiaceae	Rhodoplanes	0.2100	0.0000	0.0000
9166	Acidobacteria	Sva0725	Sva0725	unclassified	sfE	0.2046	0.0000	0.0000
7730	Proteobacteria	Deltaproteobacteria	Desulfovibrionales	Desulfohalobiaceae	Desulfonauticus	0.2045	0.0000	0.0000
9478	Proteobacteria	Alphaproteobacteria	Rhizobiales	Hyphomicrobiaceae	Hyphomicrobium	0.2033	0.0000	0.0000
7787	Proteobacteria	Deltaproteobacteria	Myxococcales	Haliangiaceae	unclassified	0.1990	0.0000	0.0000
10025	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Clostridium	0.1959	0.0000	0.0000
10664	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.1950	0.0000	0.0000
2829	Proteobacteria	Gammaproteobacteria	Alteromonadales	Shewanellaceae	Shewanella	0.1930	0.0007	0.0003
5497	Proteobacteria	Epsilonproteobacteria	Campylobacterales	Campylobacteraceae	Campylobacter	0.1921	0.0000	0.0000
10032	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Clostridium	0.1852	0.0000	0.0000
11084	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Coprococcus	0.1813	0.0000	0.0000
10341	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Ruminococcus	0.1782	0.0000	0.0000
10409	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Lachnospira	0.1743	0.0000	0.0000
9556	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Blautia	0.1681	0.0000	0.0000
9843	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Blautia	0.1634	0.0003	0.0001
9594	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.1580	0.0002	0.0001
3648	Proteobacteria	Gammaproteobacteria	Legionellales	Legionellaceae	unclassified	0.1577	0.0000	0.0000
9913	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	Clostridium	0.1566	0.0000	0.0000
2105	Proteobacteria	Gammaproteobacteria	Aeromonadales	Aeromonadaceae	Aeromonas	0.1493	0.0000	0.0000
6797	Acidobacteria	RB25	unclassified	unclassified	sfA	0.1381	0.0000	0.0000
10132	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	0.1270	0.0000	0.0000
10654	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Ruminococcus	0.1155	0.0000	0.0000
10500	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Eubacterium	0.1055	0.0000	0.0000
10435	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Coprococcus	0.0936	0.0000	0.0000
9866	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.0929	0.0000	0.0000
9828	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Roseburia	0.0858	0.0000	0.0000
6811	Proteobacteria	Epsilonproteobacteria	Campylobacterales	Helicobacteraceae	Sulfurovum	0.0749	0.0000	0.0000
10842	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.0746	0.0000	0.0000
1965	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Yersinia	0.0416	0.0000	0.0000
11125	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	0.0395	0.0000	0.0000
7845	Bacteroidetes	Bacteroidia	Bacteroidales	Porphyromonadaceae	Parabacteroides	0.0334	0.0000	0.0000
11017	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Bacteroides	0.0201	0.0000	0.0000
10303	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	0.0191	0.0000	0.0000

Table S3. Significantly enriched bacterial OTUs - Control Cecum vs. Control Cecum.

Table sorted by Fold Change. T-test p-value < 0.05, q-value < 0.07

OTU	Phylum	Class	Order	Family	Genus	Fold Change In Abundance (Cecum / Colon)	pvalue	qvalue
1965	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Yersinia	2.4057	0.0078	0.0189
7801	Proteobacteria	Deltaproteobacteria	Desulfovibrionales	Desulfovibrionaceae	Desulfovibrio	2.0880	0.0010	0.0054
5311	Synergistetes	Synergistia	Synergistales	B6	E6	2.0767	0.0044	0.0133
7405	Proteobacteria	Alphaproteobacteria	Rhodospirillales	Rhodospirillaceae	unclassified	1.7340	0.0322	0.0480
6797	Acidobacteria	RB25	unclassified	unclassified	sfA	1.6690	0.0002	0.0024
9166	Acidobacteria	Sva0725	Sva0725	unclassified	sfE	1.6208	0.0049	0.0141
7730	Proteobacteria	Deltaproteobacteria	Desulfovibrionales	Desulfohalobiaceae	Desulfonauticus	1.6067	0.0003	0.0031
9787	Proteobacteria	Alphaproteobacteria	Rhizobiales	Bradyrhizobiaceae	Bradyrhizobium	1.5828	0.0006	0.0042
733	OP3	koll11	GIF10	unclassified	sfA	1.5758	0.0008	0.0049
2011	Proteobacteria	Gammaproteobacteria	Pseudomonadales	Pseudomonadaceae	Pseudomonas	1.5312	0.0402	0.0544
8956	Proteobacteria	Deltaproteobacteria	Desulfovibrionales	Desulfovibrionaceae	Desulfovibrio	1.5253	0.0007	0.0046
3773	Spirochaetes	WWE1	PBS-18	SHA-4	W22	1.5231	0.0208	0.0349
2668	Chloroflexi	Anaerolineae	Anaerolineales	Anaerolinaceae	T78	1.5053	0.0251	0.0405
8707	Bacteroidetes	Sphingobacteria	Sphingobacteriales	Sphingobacteriaceae	unclassified	1.4680	0.0082	0.0192
1083	Actinobacteria	Actinobacteria	Bifidobacteriales	Bifidobacteriaceae	Bifidobacterium	1.4656	0.0195	0.0336
4975	Deferribacteres	Deferribacteres	Deferribacterales	Calithrixaceae	Caldithrix	1.4606	0.0422	0.0556
4159	Firmicutes	Clostridia	Clostridiales	Peptococcaceae	Desulfosporosinus	1.4418	0.0103	0.0225
10409	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Lachnospira	1.4335	0.0097	0.0215
8596	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	1.4223	0.0003	0.0028
4705	Proteobacteria	Gammaproteobacteria	Chromatiales	Ectothiorhodospiraceae	unclassified	1.4125	0.0035	0.0118
7324	Acidobacteria	Acidobacteria	Acidobacteriales	Acidobacteriaceae	unclassified	1.4093	0.0000	0.0008
3546	Proteobacteria	Deltaproteobacteria	Desulfobacterales	Nitrospinaceae	unclassified	1.4071	0.0063	0.0166
9768	Proteobacteria	Alphaproteobacteria	Rhizobiales	Hyphomicrobiaceae	Hyphomicrobium	1.3927	0.0014	0.0064
7845	Bacteroidetes	Bacteroidia	Bacteroidales	Porphyromonadaceae	Parabacteroides	1.3903	0.0335	0.0487
8394	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	1.3763	0.0058	0.0158
1567	SPAM	0319-6G9	unclassified	unclassified	sfA	1.3714	0.0010	0.0054
10858	MSBL6	EubG1	unclassified	unclassified	sfA	1.3628	0.0006	0.0042
709	Lentisphaerae	Lentisphaerae	Victivallales	Victivallaceae	unclassified	1.3416	0.0026	0.0096
1660	Chloroflexi	RA13C7	unclassified	unclassified	sfA	1.3384	0.0015	0.0064
8900	Nitrospirae	Nitrospira	Nitrospirales	FW	GOUTA7	1.3353	0.0198	0.0338
7722	Bacteroidetes	Bacteroidia	Bacteroidales	Porphyromonadaceae	unclassified	1.3268	0.0117	0.0242
5680	Spirochaetes	Spirochaetes	Spirochaetales	Spirochaetaceae	Spirochaeta	1.3174	0.0097	0.0215
2169	AC1	LC-1	unclassified	unclassified	sfA	1.3167	0.0045	0.0133
5582	Acidobacteria	Chloracidobacteria	unclassified	unclassified	sfB	1.3157	0.0457	0.0588
10617	Proteobacteria	Alphaproteobacteria	Rhizobiales	Bradyrhizobiaceae	Bradyrhizobium	1.3145	0.0016	0.0066
4553	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	1.3039	0.0069	0.0175
7842	Bacteroidetes	Bacteroidia	Bacteroidales	RikenellaceaeII	unclassified	1.3036	0.0411	0.0544
6476	Acidobacteria	Solibacteres	Solibacterales	Solibacteraceae	Candidatus Solibacter	1.2956	0.0296	0.0449
1595	Actinobacteria	Actinobacteria	Actinomycetales	Streptomycetaceae	Streptomyces	1.2785	0.0186	0.0330
9904	Proteobacteria	Alphaproteobacteria	Rickettsiales	Rickettsiaceae	Wolbachia	1.2769	0.0116	0.0242
8462	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	1.2750	0.0001	0.0018
7148	Bacteroidetes	Bacteroidia	Bacteroidales	Rikenellaceae	Alistipes	1.2737	0.0267	0.0426
3684	Fibrobacteres	Fibrobacteres	Fibrobacterales	Fibrobacteraceae	Fibrobacter	1.2710	0.0126	0.0254
11079	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Coprococcus	1.2650	0.0207	0.0349
10728	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Coprococcus	1.2606	0.0497	0.0613
5774	Proteobacteria	Epsilonproteobacteria	Campylobacterales	Helicobacteraceae	Sulfurovum	1.2589	0.0011	0.0055
7732	Cyanobacteria	Nostocophycideae	Nostocales	Nostocaceae	Dolichospermum	1.2561	0.0029	0.0101
784	Actinobacteria	Actinobacteria	Actinomycetales	Streptomycetaceae	Streptomyces	1.2560	0.0016	0.0066
4684	Proteobacteria	Betaproteobacteria	Burkholderiales	Alcaligenaceae	Achromobacter	1.2508	0.0057	0.0158
10540	Proteobacteria	Alphaproteobacteria	Rhizobiales	Bradyrhizobiaceae	Bradyrhizobium	1.2488	0.0000	0.0008
11066	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Lachnobacterium	1.2455	0.0170	0.0307
7269	Bacteroidetes	Bacteroidia	Bacteroidales	RikenellaceaeII	unclassified	1.2435	0.0011	0.0055
9719	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	1.2389	0.0291	0.0445
7200	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	1.2359	0.0027	0.0098
1857	Bacteroidetes	Sphingobacteria	Sphingobacteriales	Flexibacteraceae	unclassified	1.2323	0.0354	0.0507
7532	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	1.2225	0.0194	0.0336
2327	Proteobacteria	Gammaproteobacteria	Alteromonadales	Psychromonadaceae	Psychromonas	1.2222	0.0064	0.0166
10256	Proteobacteria	Alphaproteobacteria	Rhizobiales	Bradyrhizobiaceae	Bradyrhizobium	1.2212	0.0001	0.0011
6369	Proteobacteria	Epsilonproteobacteria	Campylobacterales	Helicobacteraceae	Helicobacter	1.2187	0.0090	0.0206
9784	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	1.2028	0.0434	0.0566
5518	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.1928	0.0280	0.0440
9901	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	1.1893	0.0026	0.0096
9489	Firmicutes	Clostridia	Clostridiales	Veillonellaceae	unclassified	1.1886	0.0339	0.0490
7384	Bacteroidetes	Bacteroidia	Bacteroidales	RikenellaceaeII	unclassified	1.1813	0.0084	0.0194
5056	Firmicutes	Clostridia	Thermoanaerobacterales	Thermoanaerobacteraceae	Caldanaerobacter	1.1740	0.0370	0.0526
7022	Acidobacteria	Solibacteres	Solibacterales	Solibacteraceae	Candidatus Solibacter	1.1702	0.0274	0.0434
8283	Proteobacteria	Alphaproteobacteria	Rhodospirillales	Rhodospirillaceae	unclassified	1.1492	0.0175	0.0313
6451	Acidobacteria	Solibacteres	Solibacterales	Solibacteraceae	Candidatus Solibacter	1.1393	0.0303	0.0457
8473	Bacteroidetes	Bacteroidia	Bacteroidales	RikenellaceaeII	unclassified	1.1375	0.0161	0.0294
1530	Actinobacteria	Actinobacteria	Actinomycetales	Nocardioidaceae	Pimelobacter	1.1258	0.0489	0.0607
9536	Proteobacteria	Alphaproteobacteria	Rhizobiales	Bradyrhizobiaceae	Bradyrhizobium	1.1133	0.0159	0.0294
4013	Proteobacteria	Betaproteobacteria	Burkholderiales	Burkholderiaceae	Ralstonia	1.1022	0.0129	0.0258
7413	Bacteroidetes	Bacteroidia	Bacteroidales	Porphyromonadaceae	unclassified	1.0999	0.0375	0.0529
5645	Spirochaetes	Spirochaetes	Spirochaetales	Spirochaetaceae	Treponema	0.8529	0.0466	0.0591

5401	Firmicutes	Bacilli	Bacillales	Paenibacillaceae	Paenibacillus	0.8454	0.0032	0.0108
3488	Proteobacteria	Gammaproteobacteria	Thiotrichales	Thiotrichaceae	unclassified	0.8408	0.0132	0.0261
10786	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	0.8379	0.0384	0.0533
1239	Actinobacteria	Actinobacteria	Actinomycetales	Intrasporangiaceae	Knoellia	0.8363	0.0384	0.0533
7790	Bacteroidetes	Flavobacteria	Flavobacteriales	Flavobacteriaceae	unclassified	0.8320	0.0286	0.0442
8002	Cyanobacteria	Nostocophycideae	Nostocales	Nostocaceae	Dolichospermum	0.8284	0.0062	0.0166
6365	Firmicutes	Bacilli	Lactobacillales	Enterococcaceae	Enterococcus	0.8249	0.0191	0.0335
8166	Cyanobacteria	Nostocophycideae	Nostocales	Nostocaceae	Dolichospermum	0.8196	0.0057	0.0158
7347	Cyanobacteria	Nostocophycideae	Nostocales	Nostocaceae	Dolichospermum	0.8148	0.0040	0.0126
88	Actinobacteria	Actinobacteria	Bifidobacteriales	Bifidobacteriaceae	Bifidobacterium	0.8058	0.0409	0.0544
7071	Spirochaetes	Spirochaetes	Spirochaetales	Spirochaetaceae	Treponema	0.8045	0.0003	0.0027
5666	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	0.7997	0.0397	0.0544
4380	Proteobacteria	Betaproteobacteria	Burkholderiales	Burkholderiaceae	Ralstonia	0.7958	0.0002	0.0024
9516	Tenericutes	Mollicutes	Entomoplasmatales	Spiroplasmataceae	Spiroplasma	0.7778	0.0005	0.0037
5961	Firmicutes	Bacilli	Bacillales	Bacillaceae	Geobacillus	0.7759	0.0150	0.0283
1041	AD3	ABS-6	unclassified	unclassified	sfA	0.7731	0.0403	0.0544
5684	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.7721	0.0479	0.0600
7136	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Pediococcus	0.7696	0.0010	0.0054
1243	Actinobacteria	Actinobacteria	Actinomycetales	Streptomycetaceae	Streptomyces	0.7603	0.0138	0.0270
6544	Firmicutes	Bacilli	Bacillales	Planococcaceae	Planomicrobium	0.7474	0.0115	0.0242
8804	Cyanobacteria	Nostocophycideae	Nostocales	Nostocaceae	Dolichospermum	0.7470	0.0000	0.0006
5428	Firmicutes	Bacilli	Bacillales	Paenibacillaceae	Paenibacillus	0.7458	0.0328	0.0484
2833	Proteobacteria	Gammaproteobacteria	Vibrionales	Vibrionaceae	Vibrio	0.7413	0.0330	0.0484
5829	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	0.7395	0.0250	0.0405
8403	Cyanobacteria	Nostocophycideae	Nostocales	Nostocaceae	Dolichospermum	0.7350	0.0056	0.0158
6379	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.7337	0.0041	0.0126
5276	Proteobacteria	Gammaproteobacteria	Alteromonadales	Alteromonadaceae	Alteromonas	0.7302	0.0071	0.0175
8246	Bacteroidetes	Bacteroidia	Bacteroidales	RikenellaceaeII	unclassified	0.7293	0.0038	0.0126
9995	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Ruminococcus	0.7264	0.0107	0.0228
5839	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	0.7217	0.0244	0.0402
9826	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	Clostridium	0.7089	0.0151	0.0283
7112	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	0.7086	0.0002	0.0026
10931	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.6988	0.0067	0.0172
6726	Firmicutes	Bacilli	Bacillales	Bacillaceae	Geobacillus	0.6936	0.0025	0.0095
6572	Firmicutes	Bacilli	Bacillales	Bacillaceae	Geobacillus	0.6906	0.0043	0.0131
8685	Cyanobacteria	Nostocophycideae	Nostocales	Nostocaceae	Trichormus	0.6891	0.0000	0.0005
9783	Firmicutes	Clostridia	Clostridiales	Clostridiales Family XIII. Incertae Sedis	Eubacterium	0.6753	0.0015	0.0064
5947	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.6751	0.0142	0.0274
10836	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	Clostridium	0.6747	0.0001	0.0020
6115	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	0.6676	0.0405	0.0544
6502	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	0.6599	0.0012	0.0060
7080	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.6573	0.0465	0.0591
4910	Proteobacteria	Gammaproteobacteria	Pseudomonadales	Moraxellaceae	Moraxella	0.6556	0.0104	0.0225
4083	Proteobacteria	Betaproteobacteria	Burkholderiales	Burkholderiaceae	Ralstonia	0.6488	0.0126	0.0254
11011	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Shuttleworthia	0.6481	0.0081	0.0192
6646	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.6390	0.0015	0.0065
5835	Firmicutes	Bacilli	Bacillales	Paenibacillaceae	Paenibacillus	0.6362	0.0070	0.0175
6068	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	0.6317	0.0003	0.0029
6599	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	0.6235	0.0472	0.0594
2747	Proteobacteria	Gammaproteobacteria	Oceanospirillales	ZA3412c	unclassified	0.6095	0.0014	0.0064
8147	Proteobacteria	Deltaproteobacteria	Syntrophobacterales	Desulfobacteraceae	Desulfococcus	0.6089	0.0082	0.0192
7579	Acidobacteria	Acidobacteria	Acidobacteriales	Acidobacteriaceae	unclassified	0.6047	0.0001	0.0011
5730	Spirochaetes	Spirochaetes	Spirochaetales	Spirochaetaceae	IE043	0.6036	0.0146	0.0278
6923	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	0.6029	0.0024	0.0092
6913	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	0.5938	0.0007	0.0047
6402	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.5836	0.0010	0.0054
8942	Proteobacteria	Alphaproteobacteria	Rhodospirillales	Acetobacteraceae	Asaia	0.5359	0.0004	0.0031
5946	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.5350	0.0227	0.0377
6003	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	0.5341	0.0040	0.0126
6107	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	0.5067	0.0004	0.0034
6233	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.5021	0.0009	0.0052
9993	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.4910	0.0009	0.0054
6478	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	0.4856	0.0002	0.0024
6568	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	0.4846	0.0000	0.0002
6711	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	0.4726	0.0000	0.0005
5620	Firmicutes	Bacilli	Bacillales	Bacillaceae	unclassified	0.4290	0.0002	0.0024
5628	Firmicutes	Bacilli	Bacillales	Paenibacillaceae	Paenibacillus	0.4193	0.0000	0.0006
6139	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.3730	0.0443	0.0574
6515	Firmicutes	Bacilli	Bacillales	Bacillaceae	Geobacillus	0.3656	0.0017	0.0067
6543	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	0.3149	0.0283	0.0440

Table S4. Significantly enriched bacterial OTUs - Control Ileum vs. DSS Ileum. Table sorted by Fold Change. T-test p-value < 0.05, q-value < 0.07

OTU	Phylum	Class	Order	Family	Genus	Fold Change In Abundance (CNTL / DSS)	pvalue	qvalue
2754	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Pantoea	7.4878	0.0352	0.0547
8394	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	4.0474	0.0055	0.0195

9787	Proteobacteria	Alphaproteobacteria	Rhizobiales	Bradyrhizobiaceae	Bradyrhizobium	3.8208	0.0007	0.0072
7842	Bacteroidetes	Bacteroidia	Bacteroidales	RikenellaceaeII	unclassified	3.6905	0.0107	0.0259
7997	Bacteroidetes	Flavobacteria	Flavobacteriales	Cryomorphaceae	Fluviicola	3.5393	0.0380	0.0568
7200	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	2.8658	0.0044	0.0173
2236	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Leclercia	2.8145	0.0059	0.0202
9125	Bacteroidetes	Bacteroidia	Bacteroidales	Marinilabiaceae	unclassified	2.7410	0.0036	0.0154
8944	Bacteroidetes	Bacteroidia	Bacteroidales	RikenellaceaeII	unclassified	2.6886	0.0003	0.0049
1914	Bacteroidetes	Sphingobacteria	Sphingobacteriales	Flammeovirgaceae	Roseivirga	2.6815	0.0004	0.0049
5369	Proteobacteria	Betaproteobacteria	Burkholderiales	Burkholderiaceae	Burkholderia	2.6312	0.0088	0.0241
8955	Bacteroidetes	Bacteroidia	Bacteroidales	RikenellaceaeII	unclassified	2.5436	0.0043	0.0173
7276	Bacteroidetes	Bacteroidia	Bacteroidales	RikenellaceaeII	unclassified	2.4822	0.0003	0.0049
2574	Bacteroidetes	Sphingobacteria	Sphingobacteriales	Flammeovirgaceae	unclassified	2.4524	0.0003	0.0049
7136	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Pediococcus	2.4122	0.0030	0.0154
7996	Bacteroidetes	Bacteroidia	Bacteroidales	RikenellaceaeII	unclassified	2.3926	0.0001	0.0032
1824	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	2.3584	0.0092	0.0241
7609	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	2.3112	0.0009	0.0086
8462	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	2.1872	0.0027	0.0154
5750	Firmicutes	Bacilli	Bacillales	Paenibacillaceae	Paenibacillus	2.0951	0.0067	0.0214
4502	Proteobacteria	Gammaproteobacteria	Xanthomonadales	Xanthomonadaceae	unclassified	2.0839	0.0200	0.0406
8235	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	1.9572	0.0003	0.0049
7532	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	1.9467	0.0001	0.0032
9683	Caldiserica	OP5	LF045	062DZ04	unclassified	1.9351	0.0108	0.0259
7699	Bacteroidetes	Bacteroidia	Bacteroidales	Porphyromonadaceae	unclassified	1.9208	0.0034	0.0154
7953	Bacteroidetes	Bacteroidia	Bacteroidales	RikenellaceaeII	unclassified	1.8450	0.0000	0.0022
8028	Bacteroidetes	Bacteroidia	Bacteroidales	RikenellaceaeII	unclassified	1.7824	0.0001	0.0032
4368	Spirochaetes	WWE1	PBS-18	SHA-4	W22	1.7206	0.0046	0.0173
4066	Proteobacteria	Betaproteobacteria	Burkholderiales	Oxalobacteraceae	unclassified	1.6867	0.0446	0.0623
3773	Spirochaetes	WWE1	PBS-18	SHA-4	W22	1.6615	0.0293	0.0505
8171	Bacteroidetes	Bacteroidia	Bacteroidales	RikenellaceaeII	unclassified	1.6540	0.0084	0.0236
8246	Bacteroidetes	Bacteroidia	Bacteroidales	RikenellaceaeII	unclassified	1.6382	0.0011	0.0097
11089	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Clostridium	1.6207	0.0072	0.0223
4109	Proteobacteria	Betaproteobacteria	Burkholderiales	Oxalobacteraceae	unclassified	1.5974	0.0006	0.0064
8597	Cyanobacteria	Synechococcophycideae	Pseudanabaenales	Pseudanabaenaceae	Pseudanabaena	1.5900	0.0170	0.0362
668	Actinobacteria	Actinobacteria	Actinomycetales	Corynebacteriaceae	Corynebacterium	1.5637	0.0001	0.0022
5791	Firmicutes	Bacilli	Bacillales	Bacillaceae	Salinibacillus	1.5623	0.0000	0.0022
8850	Gemmatimonadetes	Gemmatimonadetes	Gemmatimonadales	Gemmatimonadaceae	unclassified	1.5452	0.0284	0.0500
7269	Bacteroidetes	Bacteroidia	Bacteroidales	RikenellaceaeII	unclassified	1.5286	0.0059	0.0202
8440	Bacteroidetes	Bacteroidia	Bacteroidales	RikenellaceaeII	unclassified	1.5136	0.0016	0.0110
8685	Cyanobacteria	Nostocophycideae	Nostocales	Nostocaceae	Trichormus	1.5066	0.0010	0.0086
7727	Bacteroidetes	Bacteroidia	Bacteroidales	RikenellaceaeII	unclassified	1.4862	0.0003	0.0049
5628	Firmicutes	Bacilli	Bacillales	Paenibacillaceae	Paenibacillus	1.4748	0.0344	0.0547
5023	Proteobacteria	Betaproteobacteria	Burkholderiales	Oxalobacteraceae	unclassified	1.4644	0.0421	0.0598
8473	Bacteroidetes	Bacteroidia	Bacteroidales	RikenellaceaeII	unclassified	1.4466	0.0034	0.0154
1074	Actinobacteria	Actinobacteria	Actinomycetales	Streptomycetaceae	Streptomyces	1.4441	0.0288	0.0501
10686	CD12	MB-B2-116	unclassified	unclassified	sfB	1.4298	0.0017	0.0111
7976	Bacteroidetes	Bacteroidia	Bacteroidales	RikenellaceaeII	unclassified	1.4054	0.0015	0.0106
6451	Acidobacteria	Solibacteres	Solibacterales	Solibacteraceae	Candidatus Solibacter	1.3851	0.0353	0.0547
8714	Bacteroidetes	Bacteroidia	Bacteroidales	RikenellaceaeII	unclassified	1.3666	0.0077	0.0231
5826	Firmicutes	Bacilli	Bacillales	Planococcaceae	Sporosarcina	1.3372	0.0343	0.0547
10485	Tenericutes	Mollicutes	Entomoplasmatales	Spiroplasmataceae	Spiroplasma	1.3323	0.0222	0.0431
5046	Verrucomicrobia	Verrucomicrobiae	Verrucomicrobiales	unclassified	sfH	1.3031	0.0173	0.0365
9783	Firmicutes	Clostridia	Clostridiales	Clostridiales Family XIII. Incertae Sedis	Eubacterium	1.2804	0.0098	0.0246
467	Lentisphaerae	Lentisphaerae	Victivallales	Victivallaceae	unclassified	1.2719	0.0419	0.0598
408	Verrucomicrobia	Verrucomicrobiae	Verrucomicrobiales	Verrucomicrobiaceae	unclassified	1.2565	0.0452	0.0627
7872	Proteobacteria	Deltaproteobacteria	Desulfovibrionales	Desulfovibrionaceae	unclassified	1.1892	0.0459	0.0632
9516	Tenericutes	Mollicutes	Entomoplasmatales	Spiroplasmataceae	Spiroplasma	1.1840	0.0122	0.0278
340	VHS-B3-43	unclassified	unclassified	unclassified	sfA	1.1660	0.0314	0.0528
7731	Bacteroidetes	Bacteroidia	Bacteroidales	Porphyromonadaceae	unclassified	1.1566	0.0245	0.0451
7022	Acidobacteria	Solibacteres	Solibacterales	Solibacteraceae	Candidatus Solibacter	1.1448	0.0034	0.0154
9109	Bacteroidetes	Bacteroidia	Bacteroidales	RikenellaceaeII	unclassified	1.1354	0.0137	0.0306
7384	Bacteroidetes	Bacteroidia	Bacteroidales	RikenellaceaeII	unclassified	1.1051	0.0383	0.0568
1478	Actinobacteria	Actinobacteria	Actinomycetales	Streptomycetaceae	Streptomyces	0.8909	0.0095	0.0242
1552	Actinobacteria	Actinobacteria	Actinomycetales	Micromonosporaceae	unclassified	0.8796	0.0249	0.0451
10339	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.8460	0.0122	0.0278
9760	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Clostridium	0.8449	0.0041	0.0171
2169	AC1	LC-1	unclassified	unclassified	sfA	0.8447	0.0102	0.0253
5954	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.8270	0.0198	0.0406
8283	Proteobacteria	Alphaproteobacteria	Rhodospirillales	Rhodospirillaceae	unclassified	0.8159	0.0030	0.0154
2668	Chloroflexi	Anaerolineae	Anaerolineales	Anaerolinaceae	T78	0.8083	0.0354	0.0547
10902	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	0.8070	0.0077	0.0231
7053	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.8044	0.0359	0.0547
6123	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	0.8025	0.0465	0.0634
10665	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.8013	0.0216	0.0431
5029	Firmicutes	Clostridia	Clostridiales	Dehalobacteriaceae	Dehalobacterium	0.7939	0.0013	0.0105
1024	Actinobacteria	Actinobacteria	Actinomycetales	Cellulomonadaceae	unclassified	0.7867	0.0412	0.0598
6756	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.7796	0.0279	0.0496
1054	Candidatus Poribacteria	unclassified	unclassified	unclassified	sfA	0.7518	0.0047	0.0173
11079	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Coprococcus	0.7441	0.0233	0.0447

10559	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	0.7313	0.0120	0.0278
10388	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	Clostridium	0.7293	0.0221	0.0431
9697	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	0.7288	0.0094	0.0242
943	Actinobacteria	Actinobacteria	Actinomycetales	Microbacteriaceae	Microbacterium	0.7205	0.0332	0.0545
2814	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Escherichia	0.7189	0.0416	0.0598
3103	Proteobacteria	Alphaproteobacteria	Rhodobacterales	Rhodobacteraceae	Paracoccus	0.7178	0.0071	0.0223
6319	Firmicutes	Bacilli	Bacillales	Bacillaceae	unclassified	0.6941	0.0034	0.0154
7633	Proteobacteria	Alphaproteobacteria	Rhizobiales	Bartonellaceae	Bartonella	0.6879	0.0084	0.0236
5677	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.6719	0.0176	0.0366
10931	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.6643	0.0031	0.0154
9746	Firmicutes	Clostridia	Clostridiales	Clostridiales Family XIII. Incertae Sedis	Eubacterium	0.6387	0.0439	0.0619
6487	Firmicutes	Bacilli	Lactobacillales	Enterococcaceae	Enterococcus	0.6303	0.0411	0.0598
10986	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.6280	0.0006	0.0064
135	SAR406	AB16	ZA3648c	185	unclassified	0.6240	0.0033	0.0154
5157	Firmicutes	Clostridia	Clostridiales	Eubacteriaceae	Anaerofustis	0.6219	0.0020	0.0125
9901	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.6136	0.0054	0.0195
6084	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	0.6022	0.0319	0.0528
6198	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.5955	0.0358	0.0547
2827	Bacteroidetes	Sphingobacteria	Sphingobacteriales	Flammeovirgaceae	unclassified	0.5792	0.0499	0.0665
396	Actinobacteria	Actinobacteria	Bifidobacteriales	Bifidobacteriaceae	Bifidobacterium	0.5768	0.0236	0.0448
6119	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.5616	0.0061	0.0205
5811	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	0.5595	0.0264	0.0475
1822	Proteobacteria	Gammaproteobacteria	Alteromonadales	Psychromonadaceae	Psychromonas	0.5565	0.0092	0.0241
6871	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	0.5532	0.0247	0.0451
7043	Firmicutes	Bacilli	Lactobacillales	Enterococcaceae	Enterococcus	0.5522	0.0472	0.0639
2192	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Leclercia	0.5249	0.0317	0.0528
9834	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	Clostridium	0.4867	0.0117	0.0278
9730	Firmicutes	Clostridia	Clostridiales	Veillonellaceae	unclassified	0.4635	0.0222	0.0431
2009	Proteobacteria	Alphaproteobacteria	Rhodobacterales	Rhodobacteraceae	unclassified	0.4547	0.0014	0.0105
1516	Verrucomicrobia	Verrucomicrobiae	Verrucomicrobiales	Verrucomicrobiaceae	unclassified	0.4498	0.0036	0.0154
9968	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	Clostridium	0.4405	0.0000	0.0007
3329	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	0.4357	0.0241	0.0451
889	Verrucomicrobia	Verrucomicrobiae	Verrucomicrobiales	Verrucomicrobiaceae	unclassified	0.4081	0.0014	0.0105
3381	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	0.4046	0.0170	0.0362
321	Actinobacteria	Actinobacteria	Bifidobacteriales	Bifidobacteriaceae	Bifidobacterium	0.4006	0.0349	0.0547
10025	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Clostridium	0.3657	0.0031	0.0154
2004	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Yersinia	0.3467	0.0082	0.0236
6139	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.3362	0.0375	0.0565
2176	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Escherichia	0.2691	0.0090	0.0241
10584	Proteobacteria	Alphaproteobacteria	unclassified	unclassified	sfH	0.2628	0.0045	0.0173
2043	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Escherichia	0.2572	0.0031	0.0154
10435	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Coprococcus	0.2518	0.0311	0.0528
9442	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.2476	0.0064	0.0210
2859	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Klebsiella	0.2395	0.0166	0.0362
3394	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	0.2230	0.0168	0.0362
2264	Proteobacteria	Gammaproteobacteria	Aeromonadales	Aeromonadaceae	Aeromonas	0.2211	0.0079	0.0231
10873	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	Clostridium	0.0397	0.0004	0.0049

Table S5. Significantly enriched bacterial OTUs - DSS Ileum vs. MSC Ileum. Table sorted by Fold Change. T-test p-value < 0.05, q-value < 0.07

OTU	Phylum	Class	Order	Family	Genus	Fold Change In Abundance (DSS / MSC)	pvalue	qvalue
1516	Verrucomicrobia	Verrucomicrobiae	Verrucomicrobiales	Verrucomicrobiaceae	unclassified	2.4484	0.0002	0.0619

Table S6. Significantly enriched bacterial OTUs - DSS Cecum vs. MSC Cecum. Table sorted by Fold Change. T-test p-value < 0.05, q-value < 0.08

OTU	Phylum	Class	Order	Family	Genus	Fold Change In Abundance (MSC / DSS)	pvalue	qvalue
406	Actinobacteria	Actinobacteria	Actinomycetales	Streptomycetaceae	Streptomyces	1.4396	0.0003	0.0771
9787	Proteobacteria	Alphaproteobacteria	Rhizobiales	Bradyrhizobiaceae	Bradyrhizobium	0.4713	0.0008	0.0771
7413	Bacteroidetes	Bacteroidia	Bacteroidales	Porphyromonadaceae	Unclassified	0.7893	0.0009	0.0771

Table S7. Significantly enriched bacterial OTUs - DSS Colon vs. MSC Colon. Table sorted by Fold Change. T-test p-value < 0.05, q-value < 0.41

OTU	Phylum	Class	Order	Family	Genus	Fold Change In Abundance (DSS / MSC)	pvalue	qvalue
3884	Firmicutes	Clostridia	Clostridiales	Syntrophomonadaceae	Syntrophomonas	2.3562	0.0172	0.4004
10873	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	Clostridium	2.3375	0.0380	0.4061
9787	Proteobacteria	Alphaproteobacteria	Rhizobiales	Bradyrhizobiaceae	Bradyrhizobium	2.2645	0.0199	0.4004
10242	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Ruminococcus	2.1695	0.0008	0.2020
10768	Proteobacteria	Alphaproteobacteria	Rhizobiales	Bradyrhizobiaceae	Bradyrhizobium	2.0296	0.0230	0.4004
10500	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Eubacterium	1.7156	0.0196	0.4004
9866	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	1.6223	0.0169	0.4004
2004	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Yersinia	1.5995	0.0438	0.4061
431	Planctomycetes	Phycisphaerae	Phycisphaerales	unclassified	sfB	1.5924	0.0079	0.4004
10664	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	1.5742	0.0373	0.4061
11125	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	1.5681	0.0402	0.4061
10948	Firmicutes	Clostridia	Clostridiales	Thermoanaerobacterales Family III. Incertae Sedis	Thermoanaerobacterium	1.5371	0.0047	0.4004
9843	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Blautia	1.5065	0.0130	0.4004
9981	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Ruminococcus	1.4877	0.0070	0.4004
9203	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	1.4222	0.0061	0.4004
10788	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Butyrivibrio	1.3602	0.0270	0.4004
10379	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Coprococcus	1.3598	0.0461	0.4061
10508	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	1.3454	0.0422	0.4061
10828	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	1.2922	0.0107	0.4004
10838	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	1.2750	0.0489	0.4061
716	Actinobacteria	Actinobacteria	Acidimicrobiales	CL500-29	unclassified	1.1864	0.0263	0.4004
322	Actinobacteria	Actinobacteria	Actinomycetales	Streptomycetaceae	Streptomyces	1.1571	0.0237	0.4004
10805	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.8883	0.0477	0.4061
9536	Proteobacteria	Alphaproteobacteria	Rhizobiales	Bradyrhizobiaceae	Bradyrhizobium	0.8344	0.0366	0.4061
8923	Bacteroidetes	Bacteroidia	Bacteroidales	RikenellaceaeII	unclassified	0.8196	0.0011	0.2020
7091	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.8163	0.0398	0.4061
5389	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.8124	0.0474	0.4061
6947	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.7819	0.0160	0.4004
943	Actinobacteria	Actinobacteria	Actinomycetales	Microbacteriaceae	Microbacterium	0.7765	0.0096	0.4004
7797	Proteobacteria	Deltaproteobacteria	unclassified	unclassified	sfH	0.7760	0.0251	0.4004
4910	Proteobacteria	Gammaproteobacteria	Pseudomonadales	Moraxellaceae	Moraxella	0.7749	0.0288	0.4061
1567	SPAM	0319-6G9	unclassified	unclassified	sfA	0.7669	0.0213	0.4004
2463	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Escherichia	0.7616	0.0082	0.4004
5444	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.7610	0.0388	0.4061
10877	Cyanobacteria	Chloroplast	Streptophyta	unclassified	sfA	0.7394	0.0125	0.4004
5930	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.7214	0.0218	0.4004
7378	Proteobacteria	Deltaproteobacteria	Syntrophobacterales	Syntrophobacteraceae	unclassified	0.7078	0.0343	0.4061
667	Chloroflexi	Dehalococcoidetes	Dehalogenimonales	Dehalogenimonaceae	Dehalogenimonas	0.6615	0.0371	0.4061
2043	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Escherichia	0.6540	0.0325	0.4061
3362	Proteobacteria	Gammaproteobacteria	Alteromonadales	Shewanellaceae	Shewanella	0.6489	0.0182	0.4004

Table S8. Significantly enriched bacterial OTUs - DSS Ileum vs. VSL#3 Ileum. Table sorted by Fold Change. T-test p-value < 0.05, q-value < 0.07

OTU	Phylum	Class	Order	Family	Genus	Fold Change In Abundance (DSS / VSL)	pvalue	qvalue
7842	Bacteroidetes	Bacteroidia	Bacteroidales	RikenellaceaeII	unclassified	4.9087	0.0093	0.0331
1366	BRC1	PRR-11	unclassified	unclassified	sfA	2.6269	0.0172	0.0448
6115	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	2.6025	0.0177	0.0448
6543	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	2.3350	0.0468	0.0645
6546	Firmicutes	Bacilli	Lactobacillales	Carnobacteriaceae	Desemzia	2.2476	0.0217	0.0489
6711	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	2.1720	0.0248	0.0513
5400	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	2.0041	0.0343	0.0546
6575	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	1.9550	0.0046	0.0239
8086	Proteobacteria	Alphaproteobacteria	Caulobacterales	Caulobacteraceae	Brevundimonas	1.9346	0.0091	0.0331
322	Actinobacteria	Actinobacteria	Actinomycetales	Streptomycetaceae	Streptomyces	1.8998	0.0006	0.0081
10821	Tenericutes	Mollicutes	Entomoplasmatales	Spiroplasmataceae	Spiroplasma	1.8993	0.0132	0.0396
6322	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	1.8960	0.0293	0.0527
1041	AD3	ABS-6	unclassified	unclassified	sfA	1.8921	0.0224	0.0489
5628	Firmicutes	Bacilli	Bacillales	Paenibacillaceae	Paenibacillus	1.8549	0.0101	0.0350
6003	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.8261	0.0260	0.0526
6997	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.8082	0.0196	0.0486
9655	Tenericutes	Mollicutes	Acholeplasmatales	Acholeplasmataceae	Phytoplasma	1.7775	0.0175	0.0448
7043	Firmicutes	Bacilli	Lactobacillales	Enterococcaceae	Enterococcus	1.7719	0.0351	0.0552
6913	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	1.7598	0.0416	0.0610
5750	Firmicutes	Bacilli	Bacillales	Paenibacillaceae	Paenibacillus	1.7482	0.0299	0.0527
8147	Proteobacteria	Deltaproteobacteria	Syntrophobacterales	Desulfobacteraceae	Desulfococcus	1.7463	0.0115	0.0359
6478	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	1.7324	0.0292	0.0527
1054	Poribacteria	unclassified	unclassified	unclassified	sfA	1.7195	0.0440	0.0634
467	Lentisphaerae	Lentisphaerae	Victivallales	Victivallaceae	unclassified	1.7072	0.0343	0.0546
11099	Tenericutes	Erysipelotrichi	Erysipelotrichales	Erysipelotrichaceae	PSB-M-3	1.6971	0.0226	0.0489
6068	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	1.6756	0.0381	0.0570
7074	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	1.6537	0.0242	0.0513
5826	Firmicutes	Bacilli	Bacillales	Planococcaceae	Sporosarcina	1.6389	0.0080	0.0308
7071	Spirochaetes	Spirochaetes	Spirochaetales	Spirochaetaceae	Treponema	1.6121	0.0208	0.0489
5853	Firmicutes	Bacilli	Bacillales	Paenibacillaceae	Paenibacillus	1.6004	0.0435	0.0631
4083	Proteobacteria	Betaproteobacteria	Burkholderiales	Burkholderiaceae	Ralstonia	1.5804	0.0250	0.0513
6515	Firmicutes	Bacilli	Bacillales	Bacillaceae	Geobacillus	1.5748	0.0161	0.0435
4075	Bacteroidetes	Sphingobacteria	Sphingobacteriales	Saprospiraceae	Aureispira	1.5697	0.0496	0.0654
1368	Actinobacteria	Actinobacteria	Actinomycetales	Streptomycetaceae	Streptomyces	1.5528	0.0048	0.0240
10012	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	1.5463	0.0498	0.0654
5842	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.5386	0.0307	0.0527
10686	CD12	MB-B2-116	unclassified	unclassified	sfB	1.5293	0.0198	0.0486
5666	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	1.5047	0.0246	0.0513
10140	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	1.5024	0.0329	0.0535
9579	Tenericutes	Erysipelotrichi	Erysipelotrichales	Erysipelotrichaceae	Pei061	1.4944	0.0219	0.0489
10559	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	1.4784	0.0300	0.0527
5444	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.4742	0.0031	0.0188
8895	Actinobacteria	Actinobacteria	Solirubrobacterales	Conexibacteraceae	unclassified	1.4412	0.0372	0.0569
9918	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	1.4347	0.0472	0.0645
9489	Firmicutes	Clostridia	Clostridiales	Veillonellaceae	unclassified	1.4305	0.0142	0.0408
10513	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	1.4216	0.0014	0.0121
9475	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	unclassified	1.4138	0.0497	0.0654
11140	Firmicutes	Clostridia	Clostridiales	Veillonellaceae	Selenomonas	1.4074	0.0369	0.0569
4048	Proteobacteria	Gammaproteobacteria	unclassified	unclassified	sfE	1.3879	0.0480	0.0647
10877	Cyanobacteria	Chloroplast	Streptophyta	unclassified	sfA	1.3811	0.0089	0.0331
3186	Chloroflexi	Anaerolineae	Anaerolineales	Anaerolinaceae	Anaerolinea	1.3793	0.0369	0.0569
9516	Tenericutes	Mollicutes	Entomoplasmatales	Spiroplasmataceae	Spiroplasma	1.3702	0.0017	0.0133
6298	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.3532	0.0306	0.0527
858	Actinobacteria	Actinobacteria	Actinomycetales	Streptomycetaceae	Streptomyces	1.3459	0.0109	0.0358
10589	Proteobacteria	Alphaproteobacteria	Rickettsiales	Rickettsiaceae	Wolbachia	1.3424	0.0471	0.0645
6460	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.3413	0.0317	0.0527
8714	Bacteroidetes	Bacteroidia	Bacteroidales	RikenellaceaeII	unclassified	1.3365	0.0286	0.0527
7579	Acidobacteria	Acidobacteria	Acidobacteriales	Acidobacteriaceae	unclassified	1.3193	0.0315	0.0527
10661	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	Clostridium	1.3166	0.0285	0.0527
6308	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.2881	0.0464	0.0645
10599	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Clostridium	1.2853	0.0272	0.0527
6856	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.2661	0.0474	0.0645
10805	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	1.2660	0.0163	0.0435
11139	Proteobacteria	Alphaproteobacteria	Rhizobiales	Bradyrhizobiaceae	unclassified	1.2407	0.0460	0.0645
9112	Gemmatimonadetes	Gemmatimonadetes	Gemmatimonadales	Gemmatimonadaceae	Gemmatimonas	1.2234	0.0159	0.0435
8473	Bacteroidetes	Bacteroidia	Bacteroidales	RikenellaceaeII	unclassified	0.7934	0.0304	0.0527
1422	Actinobacteria	Actinobacteria	Actinomycetales	Streptomycetaceae	Streptomyces	0.7883	0.0124	0.0379
5774	Proteobacteria	Epsilonproteobacteria	Campylobacterales	Helicobacteraceae	Sulfurovum	0.7663	0.0311	0.0527
5180	Proteobacteria	Gammaproteobacteria	Xanthomonadales	Xanthomonadaceae	Stenotrophomonas	0.6764	0.0307	0.0527
9746	Firmicutes	Clostridia	Clostridiales	Sedis	Eubacterium	0.6336	0.0320	0.0527
10357	Chloroflexi	Ktedonobacteria	Ktedonobacteriales	Ktedonobacteraceae	Ktedonobacter	0.5637	0.0317	0.0527

4787	Proteobacteria	Gammaproteobacteria	Xanthomonadales	Xanthomonadaceae	Stenotrophomonas	0.5283	0.0038	0.0206
2801	Proteobacteria	Gammaproteobacteria	Oceanospirillales	Halomonadaceae	Portiera	0.4272	0.0071	0.0308
5369	Proteobacteria	Betaproteobacteria	Burkholderiales	Burkholderiaceae	Burkholderia	0.3864	0.0224	0.0489
2178	Proteobacteria	Gammaproteobacteria	Alteromonadales	Shewanellaceae	Shewanella	0.3655	0.0071	0.0308
5341	Proteobacteria	Betaproteobacteria	Burkholderiales	Burkholderiaceae	Burkholderia	0.3175	0.0078	0.0308
9843	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Blautia	0.3096	0.0276	0.0527
3394	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	0.2983	0.0392	0.0581
2880	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	0.2973	0.0156	0.0435
4880	Proteobacteria	Gammaproteobacteria	Pseudomonadales	Moraxellaceae	Acinetobacter	0.2563	0.0210	0.0489
7722	Bacteroidetes	Bacteroidia	Bacteroidales	Porphyromonadaceae	unclassified	0.2508	0.0036	0.0197
2814	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Escherichia	0.2339	0.0019	0.0133
2034	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	0.2178	0.0028	0.0181
2277	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Morganella	0.2143	0.0024	0.0167
3384	Proteobacteria	Gammaproteobacteria	Pasteurellales	Pasteurellaceae	Haemophilus	0.1788	0.0080	0.0308
2390	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Klebsiella	0.1733	0.0033	0.0190
2309	Proteobacteria	Gammaproteobacteria	Pasteurellales	Pasteurellaceae	Histophilus	0.1631	0.0139	0.0408
2955	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Edwardsiella	0.1329	0.0110	0.0358
1824	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	0.1301	0.0379	0.0570
1965	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Yersinia	0.1266	0.0062	0.0289
7845	Bacteroidetes	Bacteroidia	Bacteroidales	Porphyromonadaceae	Parabacteroides	0.1263	0.0050	0.0242
3338	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Regiella	0.1040	0.0073	0.0308
2196	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	0.1024	0.0011	0.0116
2631	Proteobacteria	Gammaproteobacteria	Alteromonadales	Shewanellaceae	Shewanella	0.0994	0.0012	0.0117
1817	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Enterobacter	0.0973	0.0002	0.0045
2236	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Leclercia	0.0875	0.0015	0.0121
2332	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	0.0661	0.0103	0.0350
2043	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Escherichia	0.0635	0.0002	0.0045
46	Actinobacteria	Actinobacteria	Bifidobacteriales	Bifidobacteriaceae	Bifidobacterium	0.0578	0.0221	0.0489
2192	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Leclercia	0.0545	0.0113	0.0358
2754	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Pantoea	0.0464	0.0019	0.0133
1825	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Escherichia	0.0450	0.0001	0.0021
2755	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Baumannia	0.0358	0.0029	0.0181
2264	Proteobacteria	Gammaproteobacteria	Aeromonadales	Aeromonadaceae	Aeromonas	0.0331	0.0012	0.0116
3209	Proteobacteria	Gammaproteobacteria	Aeromonadales	Aeromonadaceae	Aeromonas	0.0328	0.0007	0.0089
3329	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	0.0203	0.0003	0.0049
3381	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	0.0143	0.0001	0.0021
2859	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Klebsiella	0.0130	0.0000	0.0021
3083	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	0.0124	0.0003	0.0049
2181	Proteobacteria	Gammaproteobacteria	Alteromonadales	Shewanellaceae	Shewanella	0.0098	0.0003	0.0049
3352	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Arsenophonus	0.0091	0.0000	0.0021
2176	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Escherichia	0.0080	0.0004	0.0054
8358	Proteobacteria	Alphaproteobacteria	Sphingomonadales	Sphingomonadaceae	unclassified	0.0071	0.0076	0.0308
2679	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Enterobacter	0.0054	0.0011	0.0116

Table S9. Significantly enriched bacterial OTUs - DSS Ileum vs. DUAL Ileum. Table sorted by Fold Change. T-test p-value < 0.05, q-value < 0.04

OTU	Phylum	Class	Order	Family	Genus	Fold Change In Abundance (DUAL / DSS)	pvalue	qvalue
2679	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Enterobacter	163.3226	0.0001	0.0009
3352	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Arsenophonus	131.0012	0.0000	0.0001
2181	Proteobacteria	Gammaproteobacteria	Alteromonadales	Shewanellaceae	Shewanella	90.9257	0.0000	0.0003
2176	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Escherichia	88.3863	0.0000	0.0001
8358	Proteobacteria	Alphaproteobacteria	Sphingomonadales	Sphingomonadaceae	unclassified	75.7714	0.0004	0.0021
3083	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	70.9872	0.0001	0.0005
3381	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	65.6060	0.0000	0.0001
2859	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Klebsiella	64.3027	0.0000	0.0001
3329	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	40.7848	0.0000	0.0005
2755	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Baumannia	28.3806	0.0005	0.0026
3209	Proteobacteria	Gammaproteobacteria	Aeromonadales	Aeromonadaceae	Aeromonas	26.1114	0.0000	0.0003
2264	Proteobacteria	Gammaproteobacteria	Aeromonadales	Aeromonadaceae	Aeromonas	21.2758	0.0024	0.0063
1825	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Escherichia	19.9784	0.0000	0.0005
2192	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Leclercia	18.8779	0.0130	0.0153
2754	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Pantoea	14.6754	0.0015	0.0048
2043	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Escherichia	14.0746	0.0000	0.0005
46	Actinobacteria	Actinobacteria	Bifidobacteriales	Bifidobacteriaceae	Bifidobacterium	13.5159	0.0123	0.0149
2332	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	12.8053	0.0029	0.0068
2236	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Leclercia	10.0651	0.0012	0.0041
2196	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	9.5240	0.0021	0.0060
1817	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Enterobacter	9.0566	0.0000	0.0005

1965	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Yersinia	8.3395	0.0049	0.0093
3338	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Candidatus Regiella	7.4253	0.0113	0.0140
2631	Proteobacteria	Gammaproteobacteria	Alteromonadales	Shewanellaceae	Shewanella	7.2959	0.0169	0.0181
7081	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	7.0857	0.0075	0.0109
3384	Proteobacteria	Gammaproteobacteria	Pasteurellales	Pasteurellaceae	Haemophilus	6.7790	0.0057	0.0098
2309	Proteobacteria	Gammaproteobacteria	Pasteurellales	Pasteurellaceae	Histophilus	6.6531	0.0225	0.0215
1824	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	6.6155	0.0132	0.0153
2955	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Edwardsiella	6.3880	0.0024	0.0063
7845	Bacteroidetes	Bacteroidia	Bacteroidales	Porphyromonadaceae	Parabacteroides	5.9035	0.0090	0.0119
2277	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Morganella	4.6404	0.0002	0.0015
2390	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Klebsiella	4.5460	0.0009	0.0038
4880	Proteobacteria	Gammaproteobacteria	Pseudomonadales	Moraxellaceae	Acinetobacter	3.9748	0.0156	0.0170
2034	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	3.9134	0.0006	0.0027
9843	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Blautia	3.6088	0.0188	0.0189
2814	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Escherichia	3.5803	0.0003	0.0019
6212	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	3.3450	0.0386	0.0304
7722	Bacteroidetes	Bacteroidia	Bacteroidales	Porphyromonadaceae	unclassified	3.2430	0.0065	0.0102
5520	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	3.2049	0.0019	0.0056
2880	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	2.9879	0.0044	0.0089
5811	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	2.9839	0.0038	0.0083
6871	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	2.9732	0.0075	0.0109
3742	Proteobacteria	Gammaproteobacteria	Xanthomonadales	Xanthomonadaceae	Stenotrophomonas	2.7493	0.0048	0.0093
2004	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Yersinia	2.6850	0.0081	0.0110
5369	Proteobacteria	Betaproteobacteria	Burkholderiales	Burkholderiaceae	Burkholderia	2.3977	0.0112	0.0140
2178	Proteobacteria	Gammaproteobacteria	Alteromonadales	Shewanellaceae	Shewanella	2.3945	0.0057	0.0098
6084	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	2.2491	0.0134	0.0153
10357	Chloroflexi	Ktedonobacteria	Ktedonobacteriales	Ktedonobacteraceae	Ktedonobacter	2.1855	0.0387	0.0304
8955	Bacteroidetes	Bacteroidia	Bacteroidales	RikenellaceaeII	unclassified	2.0096	0.0117	0.0143
5646	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.8103	0.0205	0.0201
8616	Proteobacteria	Alphaproteobacteria	Sphingomonadales	Sphingomonadaceae	Sphingomonas	1.7634	0.0387	0.0304
4787	Proteobacteria	Gammaproteobacteria	Xanthomonadales	Xanthomonadaceae	Stenotrophomonas	1.6990	0.0075	0.0109
6954	Firmicutes	Bacilli	Bacillales	Bacillaceae	Lentibacillus	1.6484	0.0437	0.0334
2574	Bacteroidetes	Sphingobacteria	Sphingobacteriales	Flammeovirgaceae	unclassified	1.6029	0.0081	0.0110
709	Lentisphaerae	Lentisphaerae	Victivallales	Victivallaceae	unclassified	1.5035	0.0378	0.0304
6123	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.4918	0.0498	0.0376
9746	Firmicutes	Clostridia	Clostridiales	Clostridiales Family XIII. Incertae Sedis	Eubacterium	1.4778	0.0317	0.0277
4368	Spirochaetes	WWE1	PBS-18	SHA-4	W22	1.4562	0.0136	0.0154
1516	Verrucomicrobia	Verrucomicrobiae	Verrucomicrobiales	Verrucomicrobiaceae	unclassified	1.4110	0.0152	0.0169
406	Actinobacteria	Actinobacteria	Actinomycetales	Streptomycetaceae	Streptomyces	1.3967	0.0252	0.0232
5803	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.3917	0.0262	0.0239
10617	Proteobacteria	Alphaproteobacteria	Rhizobiales	Bradyrhizobiaceae	Bradyrhizobium	1.3183	0.0021	0.0058
6119	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.2422	0.0331	0.0283
7579	Acidobacteria	Acidobacteria	Acidobacteriales	Acidobacteriaceae	unclassified	0.8799	0.0423	0.0330
2169	AC1	LC-1	unclassified	unclassified	sfA	0.8541	0.0051	0.0093
7752	Proteobacteria	Alphaproteobacteria	Rhodospirillales	Rhodospirillaceae	unclassified	0.8194	0.0232	0.0220
834	PAUC34f	unclassified	unclassified	unclassified	sfB	0.8144	0.0356	0.0296
5842	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.7964	0.0379	0.0304
7068	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.7959	0.0029	0.0068
8714	Bacteroidetes	Bacteroidia	Bacteroidales	RikenellaceaeII	unclassified	0.7908	0.0317	0.0277
6107	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	0.7749	0.0377	0.0304
1366	BRC1	PRR-11	unclassified	unclassified	sfA	0.7748	0.0359	0.0297
9367	Firmicutes	Bacilli	Bacillales	Pasteuriaceae	unclassified	0.7697	0.0285	0.0255
5389	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.7593	0.0097	0.0124
6298	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.7539	0.0431	0.0331
7872	Proteobacteria	Deltaproteobacteria	Desulfovibrionales	Desulfovibrionaceae	unclassified	0.7535	0.0061	0.0099
10599	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Clostridium	0.7528	0.0292	0.0259
7074	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	0.7515	0.0328	0.0283
8246	Bacteroidetes	Bacteroidia	Bacteroidales	RikenellaceaeII	unclassified	0.7477	0.0368	0.0302
5629	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.7463	0.0063	0.0099
5930	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.7463	0.0324	0.0281
5428	Firmicutes	Bacilli	Bacillales	Paenibacillaceae	Paenibacillus	0.7458	0.0384	0.0304
6308	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.7385	0.0346	0.0292
9862	Tenericutes	Mollicutes	Mycoplasmatales	Mycoplasmataceae	unclassified	0.7377	0.0188	0.0189
9516	Tenericutes	Mollicutes	Entomoplasmatales	Spiroplasmataceae	Spiroplasma	0.7376	0.0027	0.0068
7413	Bacteroidetes	Bacteroidia	Bacteroidales	Porphyromonadaceae	unclassified	0.7291	0.0127	0.0152
6724	Firmicutes	Bacilli	Bacillales	Paenibacillaceae	Paenibacillus	0.7285	0.0272	0.0245
6235	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.7280	0.0164	0.0178
10877	Cyanobacteria	Chloroplast	Streptophyta	unclassified	sfA	0.7168	0.0049	0.0093
10388	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	Clostridium	0.7120	0.0095	0.0124
6264	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.7101	0.0011	0.0041
7091	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.7100	0.0076	0.0109
10513	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.7075	0.0250	0.0231
6198	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.7052	0.0183	0.0188
10902	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	0.7045	0.0240	0.0224
5444	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.7021	0.0079	0.0109
5954	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.7019	0.0051	0.0093
5947	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.7014	0.0176	0.0184
5817	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.7013	0.0088	0.0118

6822	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.7002	0.0062	0.0099
1857	Bacteroidetes	Sphingobacteria	Sphingobacteriales	Flexibacteraceae	unclassified	0.6950	0.0196	0.0194
6380	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.6943	0.0431	0.0331
5403	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.6933	0.0009	0.0038
7053	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.6915	0.0046	0.0092
6947	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.6907	0.0174	0.0184
6913	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	0.6897	0.0027	0.0068
4048	Proteobacteria	Gammaproteobacteria	unclassified	unclassified	sfE	0.6893	0.0039	0.0083
9918	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.6888	0.0144	0.0162
2747	Proteobacteria	Gammaproteobacteria	Oceanospirillales	ZA3412c	unclassified	0.6863	0.0214	0.0208
5157	Firmicutes	Clostridia	Clostridiales	Eubacteriaceae	Anaerofustis	0.6829	0.0133	0.0153
6319	Firmicutes	Bacilli	Bacillales	Bacillaceae	unclassified	0.6821	0.0040	0.0085
4998	Proteobacteria	Betaproteobacteria	Burkholderiales	Burkholderiaceae	Cupriavidus	0.6819	0.0217	0.0209
10729	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	Clostridium	0.6797	0.0061	0.0099
9724	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	Clostridium	0.6772	0.0272	0.0245
9489	Firmicutes	Clostridia	Clostridiales	Veillonellaceae	unclassified	0.6749	0.0350	0.0293
11099	Tenericutes	Erysipelotrichi	Erysipelotrichales	Erysipelotrichaceae	PSB-M-3	0.6734	0.0073	0.0109
10589	Proteobacteria	Alphaproteobacteria	Rickettsiales	Rickettsiaceae	Wolbachia	0.6732	0.0059	0.0099
6770	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.6711	0.0130	0.0153
7071	Spirochaetes	Spirochaetes	Spirochaetales	Spirochaetaceae	Treponema	0.6696	0.0037	0.0081
11140	Firmicutes	Clostridia	Clostridiales	Veillonellaceae	Selenomonas	0.6691	0.0110	0.0139
322	Actinobacteria	Actinobacteria	Actinomycetales	Streptomycetaceae	Streptomyces	0.6666	0.0076	0.0109
6839	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.6659	0.0007	0.0031
6756	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.6638	0.0030	0.0069
7070	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.6636	0.0061	0.0099
4792	Proteobacteria	Betaproteobacteria	Burkholderiales	Alcaligenaceae	unclassified	0.6563	0.0337	0.0286
5684	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.6531	0.0003	0.0019
9579	Tenericutes	Erysipelotrichi	Erysipelotrichales	Erysipelotrichaceae	Pei061	0.6473	0.0014	0.0045
10140	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.6459	0.0002	0.0015
5677	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.6451	0.0176	0.0184
6068	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	0.6440	0.0155	0.0170
2903	Proteobacteria	Gammaproteobacteria	Vibrionales	Vibrionaceae	Vibrio	0.6325	0.0066	0.0102
6322	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	0.6308	0.0012	0.0041
346	BRC1	PRR-11	unclassified	unclassified	sfA	0.6236	0.0237	0.0222
943	Actinobacteria	Actinobacteria	Actinomycetales	Microbacteriaceae	Microbacterium	0.6127	0.0052	0.0093
5287	Proteobacteria	Betaproteobacteria	Neisseriales	Neisseriaceae	Neisseria	0.6096	0.0020	0.0058
10912	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	Clostridium	0.6078	0.0180	0.0186
6408	Firmicutes	Bacilli	Bacillales	Alicyclobacillaceae	Alicyclobacillus	0.6051	0.0104	0.0133
8114	Proteobacteria	Alphaproteobacteria	Rhodospirillales	Rhodospirillaceae	unclassified	0.5999	0.0010	0.0039
1368	Actinobacteria	Actinobacteria	Actinomycetales	Streptomycetaceae	Streptomyces	0.5982	0.0003	0.0019
5628	Firmicutes	Bacilli	Bacillales	Paenibacillaceae	Paenibacillus	0.5932	0.0189	0.0189
5839	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	0.5908	0.0028	0.0068
6115	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	0.5899	0.0029	0.0068
6546	Firmicutes	Bacilli	Lactobacillales	Carnobacteriaceae	Desemzia	0.5796	0.0032	0.0073
1054	Candidatus Poribacteria	unclassified	unclassified	unclassified	sfA	0.5736	0.0053	0.0094
5985	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.5702	0.0005	0.0027
1083	Actinobacteria	Actinobacteria	Bifidobacteriales	Bifidobacteriaceae	Bifidobacterium	0.5666	0.0000	0.0005
2642	Proteobacteria	Gammaproteobacteria	Pasteurellales	Pasteurellaceae	Mannheimia	0.5621	0.0078	0.0109
8037	Proteobacteria	Alphaproteobacteria	Rhodospirillales	Rhodospirillaceae	Phaeospirillum	0.5593	0.0014	0.0046
9826	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	Clostridium	0.5205	0.0010	0.0039
5400	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	0.5189	0.0006	0.0027
6711	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	0.5180	0.0049	0.0093
5750	Firmicutes	Bacilli	Bacillales	Paenibacillaceae	Paenibacillus	0.5116	0.0191	0.0190
467	Lentisphaerae	Lentisphaerae	Victivallales	Victivallaceae	unclassified	0.4974	0.0019	0.0056
9787	Proteobacteria	Alphaproteobacteria	Rhizobiales	Bradyrhizobiaceae	Bradyrhizobium	0.4830	0.0496	0.0376
8850	Gemmatimonadetes	Gemmatimonadetes	Gemmatimonadales	Gemmatimonadaceae	unclassified	0.4599	0.0043	0.0089
1074	Actinobacteria	Actinobacteria	Actinomycetales	Streptomycetaceae	Streptomyces	0.4525	0.0077	0.0109
8086	Proteobacteria	Alphaproteobacteria	Caulobacterales	Caulobacteraceae	Brevundimonas	0.4476	0.0001	0.0006
5826	Firmicutes	Bacilli	Bacillales	Planococcaceae	Sporosarcina	0.4387	0.0006	0.0027
3103	Proteobacteria	Alphaproteobacteria	Rhodobacterales	Rhodobacteraceae	Paracoccus	0.3630	0.0000	0.0001
5029	Firmicutes	Clostridia	Clostridiales	Dehalobacteriaceae	Dehalobacterium	0.3521	0.0013	0.0045
7842	Bacteroidetes	Bacteroidia	Bacteroidales	RikenellaceaeII	unclassified	0.2610	0.0007	0.0033
9730	Firmicutes	Clostridia	Clostridiales	Veillonellaceae	unclassified	0.2590	0.0091	0.0119

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CHAPTER 3

Disease Severity and Immune Activity Relate to Inter-Kingdom Gut Microbiome States in Ethnically Distinct Ulcerative Colitis Patients

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JS Mar, BJ LaMere, DL Lin, S Levan, M Nazareth, U Mahadevan, and SV Lynch. Disease Severity and Immune Activity Relate to Inter-Kingdom Gut Microbiome States in Ethnically Distinct Ulcerative Colitis Patients. *Unpublished,* February 2016.

ABSTRACT

Significant gut microbiota heterogeneity exists amongst UC patients though the clinical implications of this variance are unknown. European and South Asian UC patients exhibit distinct disease risk alleles, many of which regulate immune function and relate to variation in gut microbiota β-diversity. We hypothesized ethnically distinct UC patients exhibit discrete gut microbiotas with unique luminal metabolic programming that influence adaptive immune responses and relate to clinical status. Using parallel bacterial 16S rRNA and fungal ITS2 sequencing of fecal samples (UC n=30; healthy n=13), we corroborated previous observations of UC-associated depletion of bacterial diversity and demonstrated significant gastrointestinal expansion of *Saccharomycetales* as a novel UC characteristic. We identified four distinct microbial community states (MCS 1-4), confirmed their existence using microbiota data from an independent UC cohort, and show they co-associate with patient ethnicity and degree of disease severity. Each MCS was predicted to be uniquely enriched for specific amino acid, carbohydrate, and lipid metabolism pathways and exhibited significant luminal enrichment of metabolic products from these pathways. Using a novel *in vitro* human DC/T-cell assay we show that DC exposure to patient fecal water led to MCS -specific changes in T-cell populations, particularly the Th1:Th2 ratio, and that patients with the most severe disease exhibited the greatest Th2 skewing. Thus, based on ethnicity, microbiome composition, and associated metabolic dysfunction, UC patients may be stratified in a clinically and immunologically meaningful manner, providing a platform for the development of FMC-focused therapy.

INTRODUCTION

Studies continue to demonstrate associations between the human microbiome (the collection of microbes and their encoded genes that reside in and on humans) and a variety of disease indications (79). Though murine and human studies provide evidence supporting the involvement of gut microbiota in the development and pathogenesis of ulcerative colitis (UC; a common form of IBD), a singular, causative agent has not been identified in humans and depletion of bacterial diversity remains the primary constant feature of UC microbial dysbiosis (27-29, 80, 81). Emerging evidence indicates distinct disease endotypes exist within clinically defined patient populations with chronic inflammatory diseases (82, 83), suggesting that, in the context of immune dysfunction, distinct pathogenic processes converge upon common clinical manifestations. Hence, combining such patients for analyses masks discrete patient sub-populations and the microbiological and/or immunological features that characterize them.

Host genetics, diet and environmental exposures, three factors encompassed by ethnicity, are known to influence UC pathology and suggests these factors may mediate their effect via changes in the gut microbiome (84-87). A large study of ethnically distinct healthy subjects located in the United States, Venezuela or Malawi demonstrated a significant relationship between ethnicity and both the composition and function of the fecal microbiota (88). Though this study indicated diet represented the strongest selective pressure on the gut microbiome of study participants, Frank *et al.* have demonstrated that Inflammatory Bowel Disease (IBD) genotype, specifically the presence of risk alleles ATG16L1 and NOD2 (associated with autophagy and host response to microbes, respectively), significantly associate with specific gut microbiome compositions (89). An independent meta-analysis of genome-wide association studies demonstrated that UC risk alleles characteristic of Caucasian populations do not confer heightened risk in ethnically distinct North Indian subjects (87, 90). These studies highlight the fact that UC is driven by a network of disease determinants known to influence the gut microbiome and suggest that ethnicity may be associated with distinct gut microbiomes in

UC populations. Based on these observations we hypothesized that distinct pathogenic microbiotas exist within UC patient cohorts and that these co-vary with both patient ethnicity and disease severity. Given the emerging evidence for gut microbial metabolic dysfunction as a characteristic of immune dysfunction (91, 92), we further hypothesized that distinct pathogenic microbiota exhibit a predictable program of luminal metabolism and elicit significantly different degrees of adaptive immune activation *in vitro*.

RESULTS

Inter-kingdom gut microbiota perturbations are characteristic of UC patients.

Our study population consisted of a cohort of 43 subjects (n=30 UC patients and n=13 healthy subjects) of self-reported European or South Asian ethnicity (see Methods and Supplemental Table 1). Several studies have examined bacterial community composition in fecal samples from UC patients however, to date, none have examined fungal members of the adult UC fecal microbiome. We therefore generated parallel high-resolution bacterial (16S rRNA) and fungal (ITS2) biomarker gene profiles from fecal material obtained from each participant, using the Illumina MiSeq platform. Our ethnically restricted UC population exhibited bacterial microbiota dysbiosis consistent with that previously described (27-29), in that they were significantly reduced in α-diversity (p=0.010; Fig. 1A) and were compositionally distinct from healthy subjects (PERMANOVA: Weighted UniFrac, R^2=0.058, p=0.023; Fig. 1B). Neither fungal α- nor β-diversity differed between healthy and UC patients (p=0.523; Fig. S1A and PERMANOVA: Bray-Curtis, R^2=0.038, p=0.129; Fig. S1B). This suggested that while profound bacterial depletion is characteristic of the UC gut microbiota, more subtle changes in fungal taxonomy characterize these patients.

To address this, we compared relative abundance of bacterial and fungal taxa (defined as ≥97% sequence similarity) across UC and healthy control subjects. A total of 165 bacterial taxa were significantly differentially enriched between healthy and UC participants (Supplemental Table 2). Consistent with previous reports (27-29)*, Bacteroides spp., Prevotella spp.,* as well as a number of unclassified *Lachnospiraceae* and *Ruminococcaceae* were amongst those bacterial taxa most significantly depleted in UC gut microbiota (Fig. 1C, Supplemental Table 2). UC patients also exhibited enrichment of members of the *Streptococcus, Bifidobacterium,* and *Enterococcus* genera (Fig. 1C, Supplemental Table 2), which were confirmed by independent phylogenetic microarray profiling of these same samples (Supplemental Table 3) and align with findings in previous reports (27-29). As predicted from our α- and β-diversity comparisons, only a small number of fungal taxa (n=13) exhibited differential relative abundance (Supplemental Table 4). UC patients were depleted of *Pleosporales, Eurotiales* and *Saccharomycetales* (including *Alternaria alternata, Aspergillus flavus, Aspergillus cibarius and Candida sojae)* and significantly enriched for distinct S*accharomycetales*, specifically *Candida albicans* and *Debaryomyces spp.*, which exhibited the greatest relative enrichment (Fig. 1D, Supplemental Table 4). Collectively, these data indicate the UC-associated gut microbiome is characterized by an inter-kingdom dysbiosis, highlighted by significant expansion of putatively pathogenic bacterial and fungal species, in the context of depleted bacterial diversity.

Figure 1.

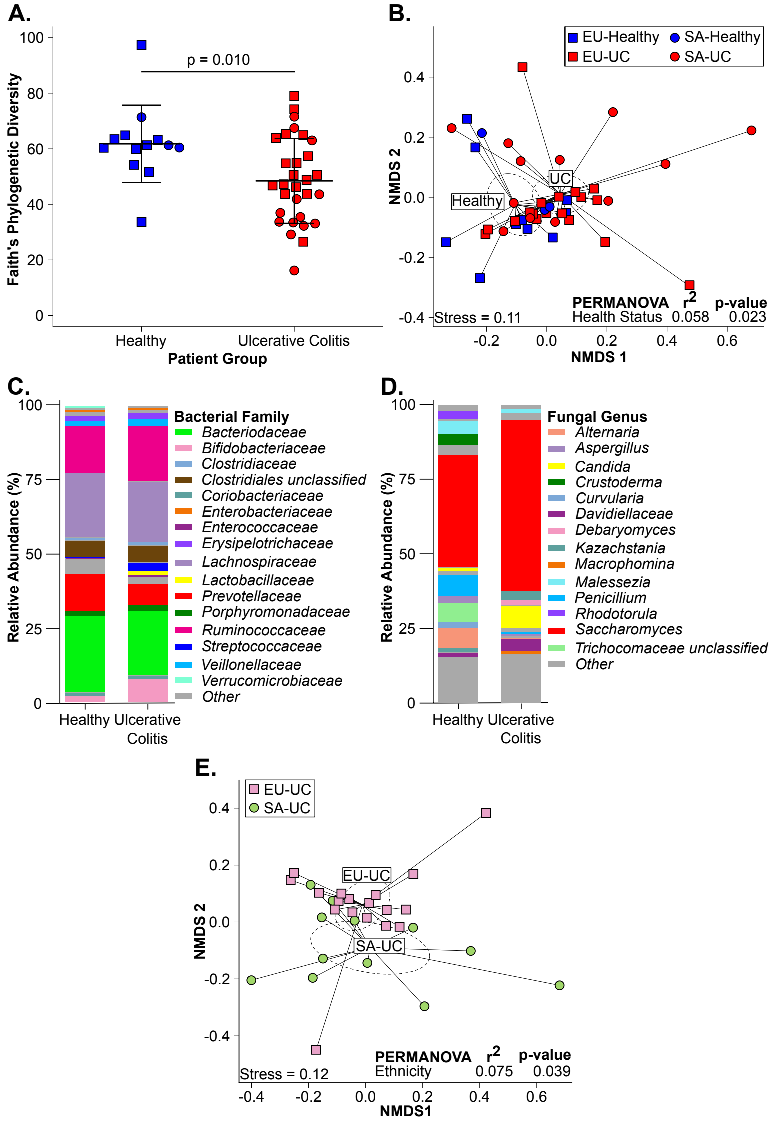

Figure 1. Comparison of the Healthy (n = 13) and UC-associated (n = 30) fecal microbiota. (A) Bacterial α-diversity. Horizontal bars represent mean +/- standard deviation. P-values obtained by two-tailed T-test. **(B)** Bacterial community composition represented by non-metric multidimensional scaling (NMDS) of pairwise Weighted UniFrac distances. Compositional bar plots of the mean, relative abundance of **(C)** bacterial families and **(D)** fungal genera. **(E)** Bacterial community composition of UC-patients stratified by ethnicity (n = 18 EU-UC, 12 SA-UC) represented by NMDS of pairwise Weighted UniFrac distances. For **(B)** and **(E)**, dashed ellipses represent the 95% CI for stratification group as calculated by *envfit.*

UC fecal microbiota segregate by ethnicity, dominant microbial features and disease characteristics.

We next addressed our initial hypothesis that ethnicity is associated with distinct inter-kingdom fecal microbiota in UC patients. Healthy EU and SA participants exhibited no significant difference in bacterial or fungal α-diversity (Fig. S2A and B). However SA-UC patients consistently exhibited depleted bacterial diversity compared to either healthy ethnically matched controls or to EU-UC patients (Fig. S2A). They also were significantly depleted of fungal diversity compared to the EU-UC group (Fig. S2B), indicating more severe inter-kingdom microbiome depletion in SA-UC patients. Of note, no difference in clinical disease severity was observed between EU- and SA-UC patients (Fig. S2C). As we had described for disease status, ethnicity was also significantly associated with bacterial, but not fungal, β-diversity when all participants were considered (Fig. S2D-E). However, because health status was significantly associated with gut microbial composition, it represented a potential confounding factor. We therefore repeated PERMANOVA using only UC patients and show that, while fungal community composition does not exhibit a significant relationship with patient ethnicity (PERMANOVA: Bray-Curtis, R^2=0.061, p=0.107), bacterial β-diversity does (PERMANOVA: Weighted UniFrac, R^2=0.075, p=0.039; Fig. 1E), an observation validated by our PhyloChip data (Fig. S3). Thus these data indicate that, despite chronic colonic inflammatory disease, ethnicity is associated with compositionally distinct bacterial communities in the UC gut, though it explains only a small proportion (7.5%) of the observed variation in microbial community composition in these patients.

Recent pediatric Crohn's studies have demonstrated that patients cluster into sub-groups based on patterns of microbial co-association (30, 93). We next asked whether such patterns exist in our adult UC cohort and relate to patient ethnicity and/or clinical correlates of disease severity. Using hierarchical cluster analysis and multi-scale, bootstrap resampling, we identified four clusters of UC patients based on fecal bacterial community composition and termed these microbial community states 1-4 (MCS1-4; Fig. 2). These distinct groups were confirmed by PERMANOVA using a weighted UniFrac distance matrix of 16S rRNA profiles generated via Illumina MiSeq as well as a Canberra distance matrix of 16S rRNA profiles generated via PhyloChip (Fig. S4A-B). MCS distribution differed significantly across ethnicities with EU-UC populations enriched for MCS1 and MCS2 compared to SA-UC patients (Fisher exact test; p=0.042; Fig. S4C).

The clinical relevance of grouping patients based on MCS was assessed using an inter-group comparison of clinical disease severity [Simple Clinical Colitis Activity (SCCA) index (94), extra-colonic manifestations (arthritis, pyoderma gangrenosum, erythema nodosum, and uveitis), number of first- and second-degree relatives diagnosed with IBD, and duration (years since UC diagnosis). MCS1 patients exhibited more severe disease with higher median SCCA scores, a significant increase in the number extra-colonic manifestations, a greater number of first- and second-degree relatives diagnosed with IBD and longer disease duration (Fig. 3). Though we recognize that the number of patients in our study is small, these data provide the first indication that distinct UC gut microbiota exist and are associated with the degree of disease severity.

Figure 2.

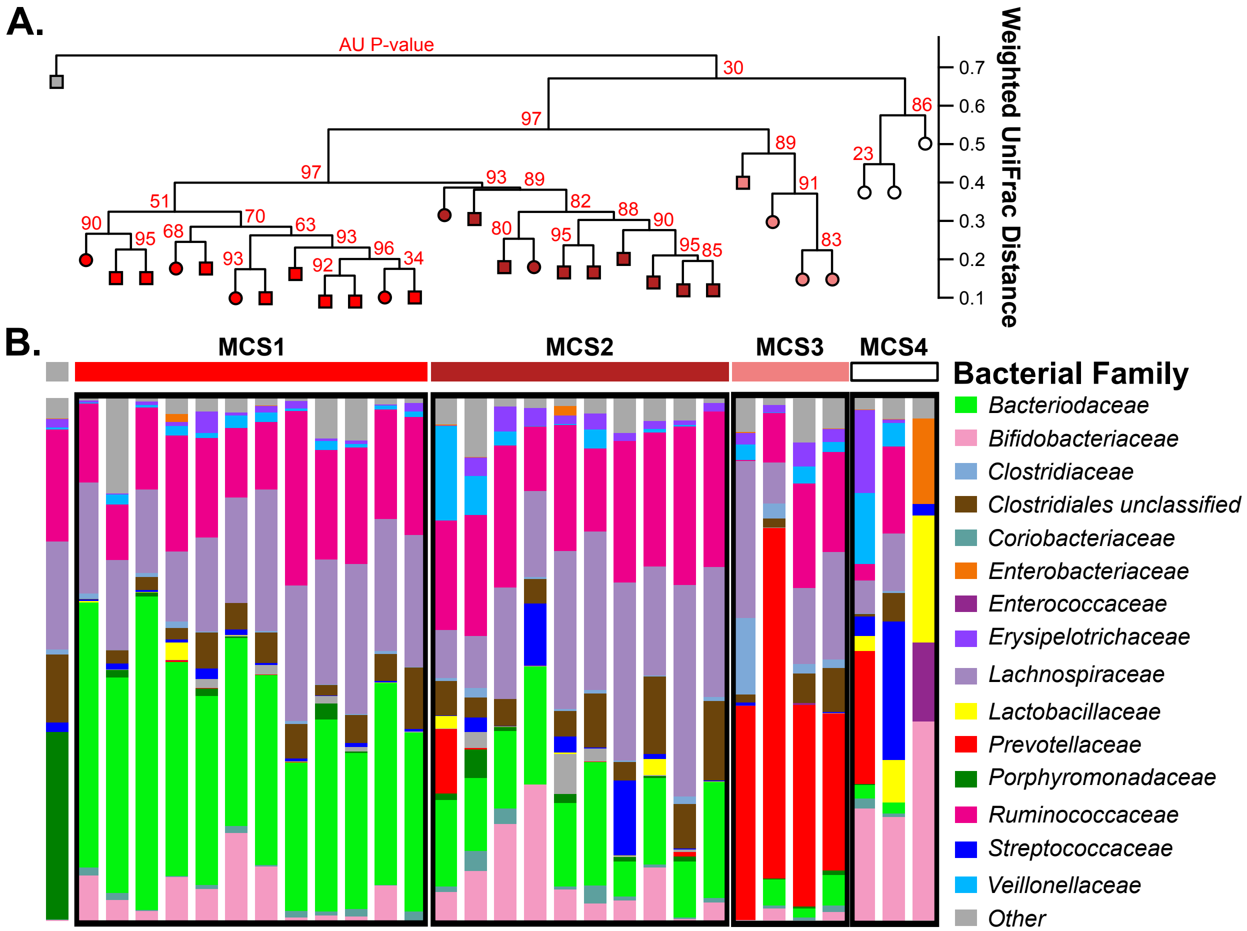

Figure 2. **Comparison of fecal bacterial communities amongst all UC patients (n = 30). (A)** Hierarchical cluster analysis using pairwise Weighted Unifrac distances. Approximately unbiased p-values (red) computed by multiscale bootstrap resampling. EU-UC (square) and SA-UC (circle). **(B)** Compositional plots of bacterial family relative abundance for each UC patient.

Figure 3.

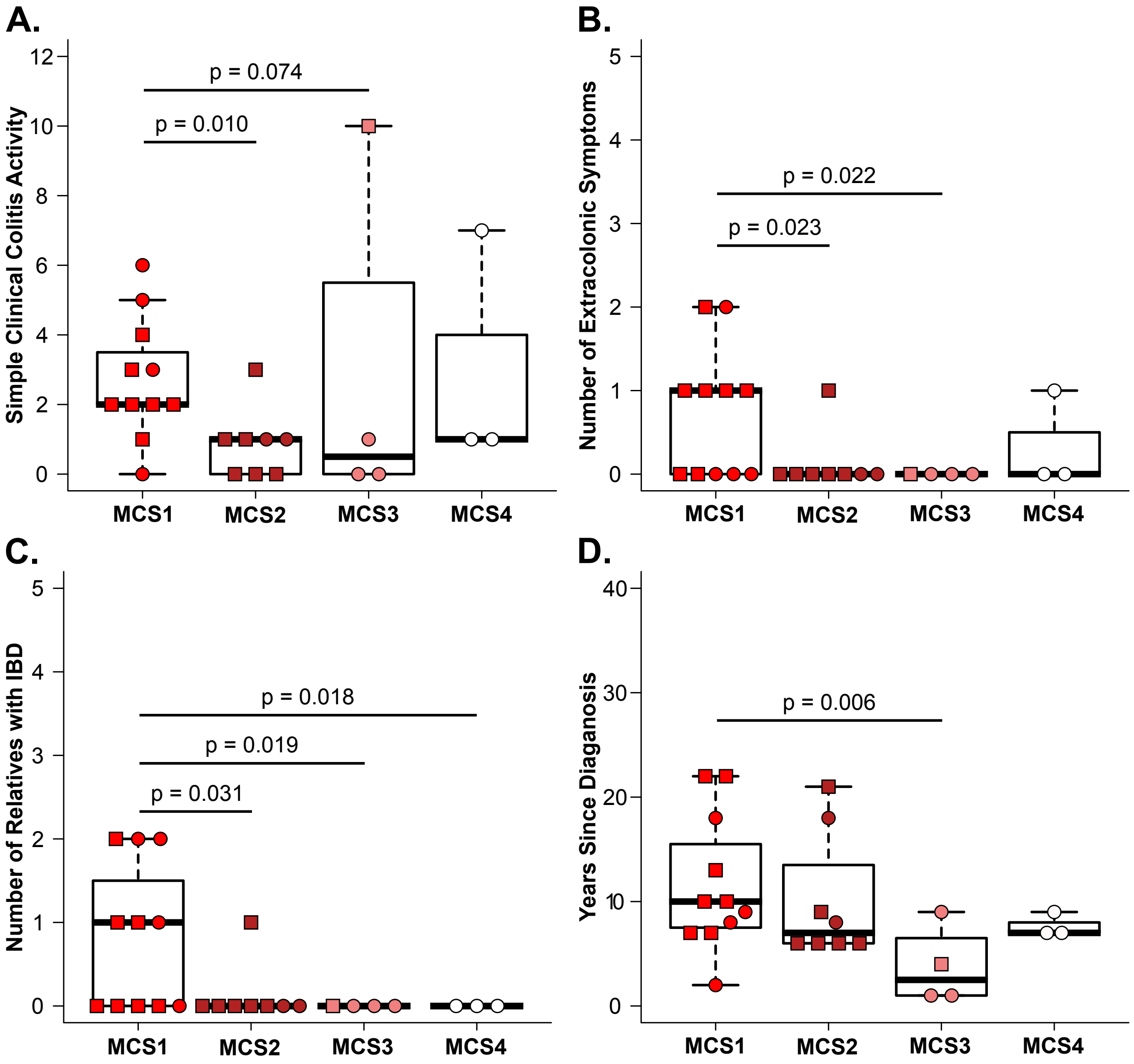

Figure 3. Clinical measures of UC severity amongst UC-MCS (n = 11 for MCS1, 8 for MCS2, 4 for MCS3, 3 for MCS4). (A) Simple Clinical Colitis Activity. **(B)** Number of extra-colonic symptoms. **(C)** Number of family members diagnosed with IBD. **(D)** Duration of disease. All pairwise p-values obtained by two-tailed Dunn's Test. Only p-values < 0.1 are indicated. EU-UC (square) and SA-UC (circle).

UC microbial community states exhibit distinct microbial composition, metagenomic capacity and metabolic productivity.

The distribution of microbial taxa across the four UC-MCS was assessed to identify the specific bacterial and fungal enrichments characteristic of each. Each MCS typically exhibited a distinct dominant bacterial family (MCS1: *Bacteroidaceae*, MCS2: *Lachnospiraceae/Ruminococcaceae*, MCS3: *Prevotellaceae*, MCS4: *Bifidobacteriaceae*; Fig. 2B & 4). These MCS specific bacterial enrichments were further emphasized when comparing the high disease severity MCS1 group with each of other three groups (MCS2, -3, and -4). Specifically, a majority of bacterial taxa enriched in MCS1, were members of the *Bacteroides* genus while MCS-2, -3, or -4 were enriched for *Blautia* and *Ruminococcus*, *Prevotella*, or *Bifidobacterium* genera respectively (Generalized Linear Models $p<0.05$, Fig. S4D, Supplemental Table 5). Using dominant bacterial family as a classifier, we validated the existence of MCS1 and -2 (the two major MCS detected predominantly in EU-UC patients) in two independent publicly available UC microbiota datasets comprised of both fecal and biopsy samples obtained from patients primarily of European descent (Fig. S5) (29, 30), thus indicating these MCS are not exclusive to our study but exist in UC patient populations nationwide. Regarding MCS specific fungal expansions, *C. albicans* and *Debaromyces spp.,* were most highly enriched in MCS1 patients compared to each of the three remaining MCS (Generalized Linear Models $p<0.05$, Supplemental Table 6), indicating an inter-kingdom expansion of *Bacteroides* and co-associated *C. albicans* and *Debaromyces* is associated with the MCS of patients with greater UC disease severity.

To identify microbiota-derived pathways and products characteristic of each MCS that may modulate host immune response and contribute to clinical disease severity, we performed *in silico* metagenomic predictions in parallel with broad-spectrum gas and liquid chromatography mass spectrometry of fecal samples. Phylogenetic Investigation of Communities by Reconstruction of Unobserved States, a bioinformatics package that predicts metagenomes from a biomarker gene such as 16S rRNA (PICRUSt; http://picrust.github.io/picrust/) (52), was used to predict bacterial functional capacity. Presently, this algorithm cannot be used to predict fungal community function. Predicted KEGG Pathways varied significantly by MCS (PERMANOVA: Bray-Curtis, R^2=0.384, p=0.002; Fig. 5A). A total of 144 bacterial KEGG pathways discriminated MCS1-4 including those involved in amino acid and lipid biosynthesis and metabolism (Kruskall Wallace q<0.0006, Supplemental Table 7, Fig. S6). Specifically, differential enrichment of glycerolipid, fatty acid, inositol, and multiple amino acid metabolism pathways, including phenylalanine, tyrosine, tryptophan, glutamate, and glutamine, differentiated these groups (Supplemental Table 7, Fig. S6). Functional predictions of UC stool samples classified as MCS1 and from the independent Morgan *et al*. and Gevers *et al*. studies (29, 30) corroborated these findings and exhibited a high degree of concordance with the predicted function of MCS1 and -2 in our study. A total of 121 pathways were differentially enriched between MCS1 and MCS2 in our study, 74 (61.2%) of which were also predicted to discriminate MCS1 from MCS2 in both the Gevers *et al*. and Morgan *et al*. data sets, indicating inter-individual conservation of bacterial function within specific UC-MCS across multiple independent studies (Supplemental Table 8).

We hypothesized that the predicted functional differences across MCS would manifest as distinct programs of luminal metabolism, particularly since the majority of pathways predicted to differentiate these communities were involved in amino acid and lipid metabolism. Each MCS exhibited significantly distinct metabolic programs (PERMANOVA: Canberra, R^2=0.209, p=0.004, Fig. 5B) that were significantly related both to the fecal microbiota present (Mantel test: r=0.38, p<0.0001; Table S9) and its predicted metagenome (Mantel test: r=0.21, p<0.008; Table S9). We were particularly interested in those luminal metabolites that discriminated the more severe MCS1 from each of the remaining MCS. Of the 805 metabolites detected across all samples, 207 exhibited significant inter-MCS differences in relative concentration (Welch's T-test p<0.05, Fig. S7, Supplemental Tables 10-12). Compared to less severe MCS groups, MCS1, as predicted by PICRUSt, was primarily characterized by altered amino acid and lipid metabolism manifest as significant enrichment of ophtalmate [a biomarker of increased oxidative stress and depleted glutathione (95, 96)], oxidative stress inducing putrescine (97, 98), pro-inflammatory p-cresol sulfate (99-101), 9- and 13-hydroxyoctadecadienoic acid [9- and 13-HODE; a pro-inflammatory, leukocyte recruiting monohydroxy fatty acids (102-105)], 9,10-dihydroxyoctadecanoic acid [9,10-DiHOME; a neutrophil recruiting, cytotoxic dihydroxy fatty acid (106-108)], as well as bioactive lysolipids involved in leukocyte activation (103, 109, 110) (Fig. 6, Supplemental Tables 10-12). In contrast, lower disease severity MCS (MCS2, -3, and -4) were enriched for a range of potentially protective dipeptides [including anti-inflammatory alanyl-glutamine (111, 112)], γ-glutamyl dipeptides indicative of improved oxidative stress coping mechanisms (113, 114), and antioxidant immunosuppressive myo-inositol (115-119). These observed differences in gut luminal metabolic programming between MCS associated with high and low UC severity indicate the existence of putative mechanisms to control inflammation in patients with less severe disease.

Figure 4.

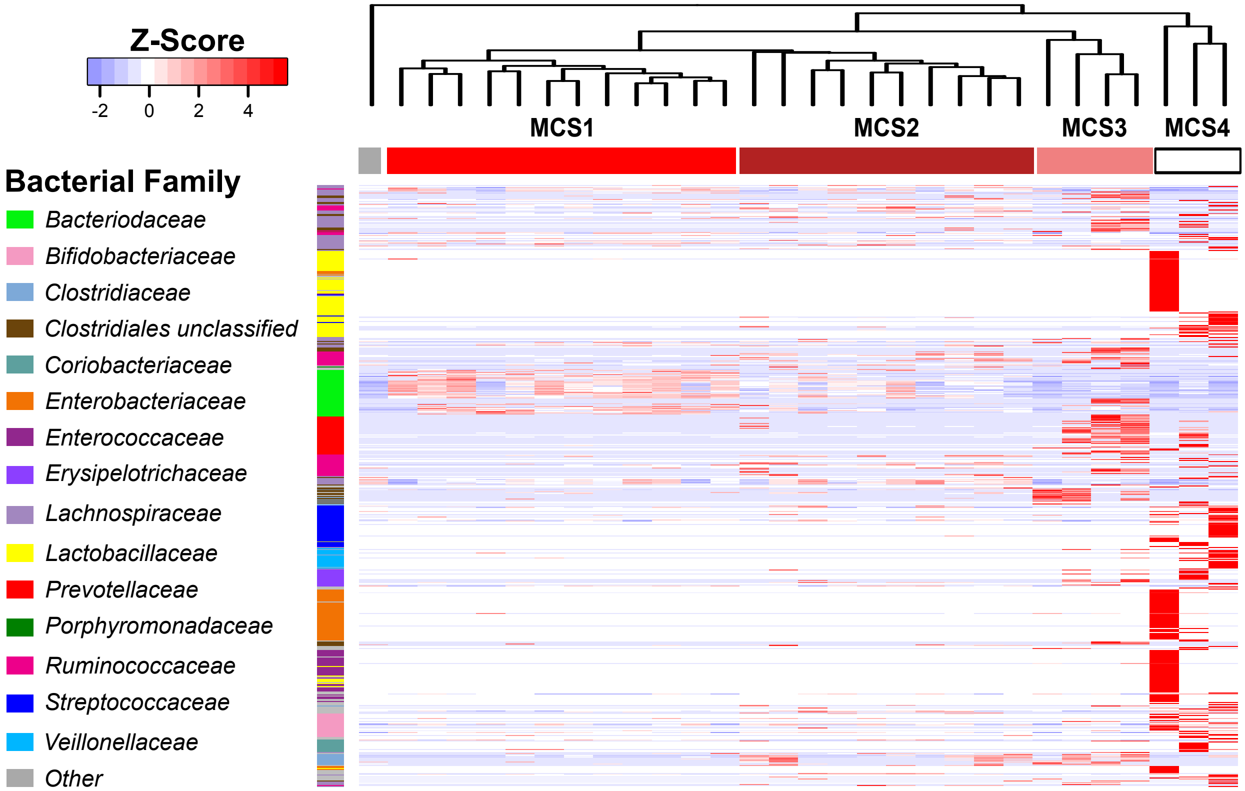

Figure 4. Heatmap of significantly enriched bacterial OTUs across UC-MCS. Depicted OTUs were identified by Kruskal-Wallis test comparing distribution amongst UC-MCS (p-value <0.05, q-value < 0.08). Column order is consistent with Fig. 2. Rows are order based on phylogenetic relatedness. For visualization, read counts were normalized [Log2(x+1)] and scaled by row.

Figure 5.

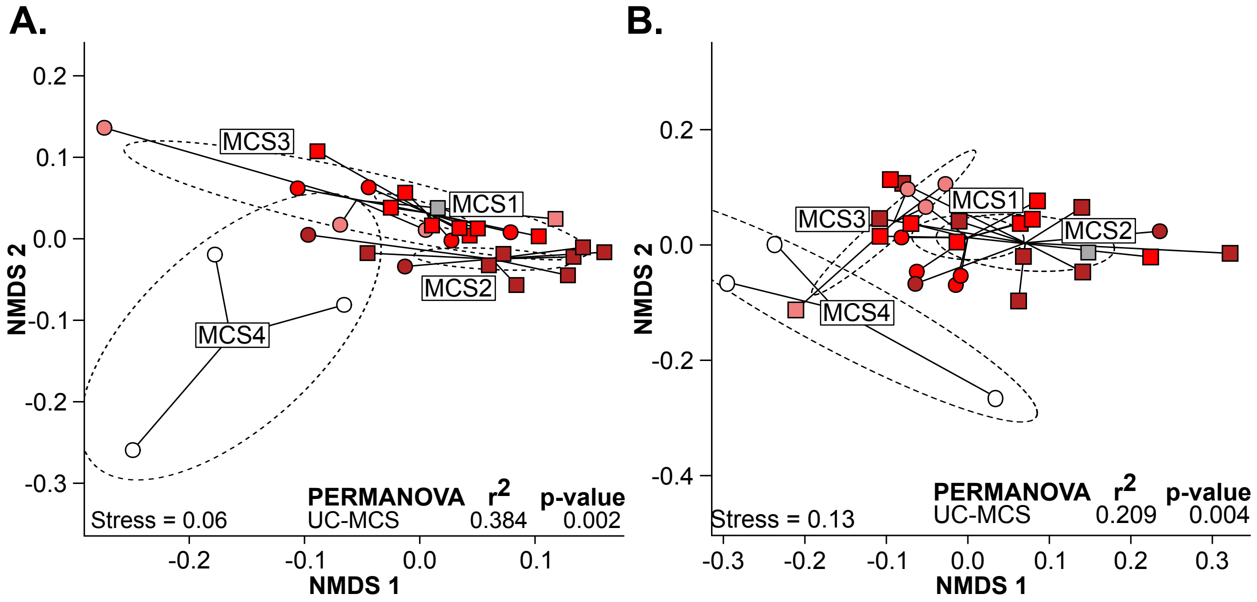

Figure 5. Comparison of predicted bacterial metagenome and associated fecal metabolome amongst UC patients stratified by UC-MCS (n = 12 for MCS1, 10 for MCS2, 4 for MCS3, 3 for MCS4, 1 Other). (A) Predicted bacterial metagenome composition of UC-patients stratified by UC-MCS represented by NMDS of pairwise Bray-Curtis distances. **(B)** Fecal metabolome composition of UC-patients stratified by UC-MCS represented by NMDS of pairwise Canberra distances. Dashed ellipses represent the 95% CI for stratification group as calculated by *envfit*. EU-UC (square) and SA-UC (circle).

T-cell activity *in vitro* is related to MCS and health status.

Recent studies have demonstrated that specific microbially derived metabolites influence Th2 responses (91), and, independently, that pro-inflammatory cytokine production by T-helper cell populations, including Th2 cells, is associated with UC (120-122). We hypothesized that distinct MCS and their associated metabolic products differentially influence T-cell activity *in vitro* in a manner consistent with disease severity. To assess this, we developed an *in vitro* assay involving co-incubation of human dendritic cells (DCs, obtained from healthy donors) with filter-sterilized fecal water prepared from study participants' feces prior to DC co-culture with autologous human T-cells. Flow cytometry was used to assess resulting T-cell phenotypes (see materials & methods for more detail). Compared to healthy participants, UC patients exhibited a significant reduction in the ratio of Th1:Th2 cells (Th2-skew; Linear mixed effects $p<0.05$; Fig. 6A), significantly increased numbers of both Th1 and Th17 cells and trends towards increases in both T-regulatory and Th2 cells (Fig. 6B-E). CD8+ T-cell subsets examined did not differ significantly between healthy participants and UC patients (Supplementary Fig S8A-C). These findings suggest luminal microbial products captured in sterile fecal water contribute to UC by inducing expansion of CD4+ T-cell populations.

Having demonstrated the Th2-skewing immunomodulatory effect of UC-associated fecal metabolites, we asked if this immune response varied based on MCS and associated differences in symptom severity, focusing specifically on Th1 and Th2 populations. With the exception of a minor significant increase in Th1 populations in response to MCS4 fecal metabolites, no significant differences in overall Th1 or Th2 cell populations were observed between MCS groups and controls (Fig. 6F and G). However when the Th1:Th2 ratio was calculated for each group, MCS1 exclusively exhibited a significant reduction in the Th1:Th2 ratio compared to healthy controls (Th2-skew; Fig. 6H). Furthermore, when considering the two MCS demonstrating the greatest difference in disease severity (MCS1 and MCS2), exposure to MCS1 fecal water induced the greatest secretion of Th2-associated cytokines (IL-4, IL-5, and IL-

13) compared the healthy controls as well (Fig. S9). These *in vitro* data provide evidence that compositionally and metabolically distinct UC-microbiota are capable of influencing T-cell populations, which, in the case of MCS1, are associated with more severe UC symptoms.

Figure 6.

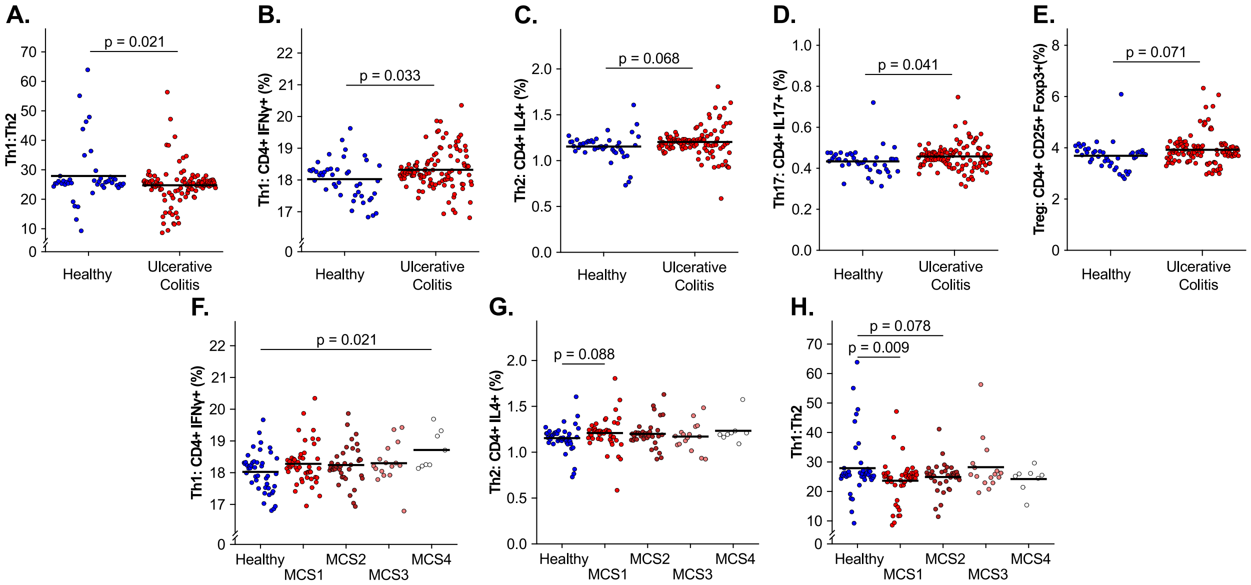

Figure 6. *In vitro* human T-cell activity following co-culture with autologous DCs challenged with sterilized fecal water. **(A)** Th1:Th2 ratio, **(B)** Th1 frequency, **(C)** Th2 frequency **(D)** Th17 frequency, and **(E)** Regulatory T-cell frequency (n = 48 Healthy, 116 UC). Comparison of **(F)** Th1:Th2 ratio, **(E)** Th1 frequency, and **(F)** Th2 frequency between Healthy and UC-MCS (n = 48 for Healthy, 48 for MCS1, 40 for MCS2, 16 for MCS3, and 8 for MCS4). Data generated from four replicate experiments using DC/T-cells obtained from four anonymous PBMC donors. Horizontal bars (mean fitted values for each group) and P-values were determined by linear mixed-effect modeling (see materials & methods).

DISCUSSION

In the context of UC, patient heterogeneity is a significant barrier to treatment efficacy. We sought to address this by determining whether ethnically distinct UC patients residing in a relatively restricted geographic area exhibited distinct gut microbiota. As a secondary analysis we hypothesized distinct but repeating patterns of microbial co-colonization existed in this patient population and explained (to a greater degree than ethnicity) host immune responses and clinical outcomes.

Preliminary analysis indicated UC-associated gut microbiota were characterized by reduced bacterial diversity and a significant enrichment of two *Saccharomycetales* family members: *C. albicans* and *Debaromyces spp*. *Saccharomycetales* enrichment has recently been described in three independent studies of the gut microbiota in adult Crohn's disease, pediatric Crohn's disease, and pediatric IBD (Crohn's and UC patients combined) (93, 123, 124), indicating fungal expansion in the context of a depleted bacterial microbiota is a consistent feature of IBD in pediatric and adult populations. Furthermore, *C. albicans* colonization has been shown to impair GI healing in both UC patients and a murine model of UC (125), suggesting fungal expansion in the gut actively contributes to UC pathology.

Though considerable variation in fecal microbiota composition was observed amongst UC patients, a proportion of this variation was explained by patient ethnicity (7.5%). This represented a much smaller proportion of variance compared to that explained by ethnicity in previous comparisons of US, Malawian and Amerindian populations' microbiomes (88), indicating additional factors influence community composition in UC patients. Substantial evidence exists for microbial inter-species interactions that deterministically influence microbial co-associations, physiology and behavior (126, 127). For example, *C. albicans* is known to co-aggregate with a variety of bacterial species in the oral microbiota, facilitating more robust and stress resistant mixed-species biofilms. In turn, the products of these co-associated bacterial species induce a physiological shift towards a yeast form in *C. albicans* (126). Similarly, *Streptococcus gordonii* facilitates *Fusobacterium nucleatum* co-association via metabolic cross-feeding (127). Considering inter-species microbial interactions may lead to deterministic patterns of microbial co-association in perturbed UC microbiota, we examined whether distinct but repeatable patterns of bacterial community composition existed in this population. Four distinct microbial community states (MCS1-4) were evident and differed significantly in their prevalence along ethnic divides. Internal validation confirmed these MCS were not an artifact of our profiling and analysis techniques. External validation using data from two independent UC microbiota studies confirmed the existence of MCS1 and 2, the two most common microbiota states found in our study. This indicates that, despite the inherent variability in patients, treatment regimes, and geography, relatively conserved microbiota states exist across UC populations within the USA

Of the four MCS identified in our study, MCS1 exhibited a more severe clinical pathology, suggesting the composition and activities of this MCS may enhance immune activation and disease severity. MCS1 characteristically exhibited overt expansion of *Bacteroides spp.*, which have been shown to produce enterotoxin previously associated with UC (128), stimulate IL-8 and TNF-α secretion in intestinal epithelial cells (129), and intensify colitis symptoms in a murine model of UC (130, 131). MCS1 patients also exhibited the greatest expansion of *C. albicans* and *Deboramyces,* implicating fungal activities in more severe UC disease. Conversely, *Blautia spp.* (enriched in MCS2) have been associated with reduced inflammation in Graph Versus Host Disease (132) and, along with *Ruminococcus spp.* (also enriched in MCS), can produce anti-inflammatory short chain fatty acids (24, 25, 42, 133-135). *Prevotella spp.* (enriched in MCS3) are capable of suppressing lymphocyte activity while *Bifidobacterium spp.* (enriched in MCS4) have been shown to reduce both IL-8 and TNF-α production in intestinal epithelial cells (136-139). While the shared detection of MCS in both our and independent UC microbiota datasets indicates the durability of these microbial states, their long-term stability cannot be assessed with our data. Additionally, it is likely the identified MCS represent discrete points along a non-linear continuum of microbial successional states that relate to disease progression and severity, similar to the microbial gradient identified by Gevers *et al.* for pediatric Crohn's disease (30). More expansive, longitudinal studies containing intra-personal repeated measures could further address both these topics.

While inter-kingdom microbial taxonomic states may be informative as a stratification tool in larger, longitudinal studies, we postulated the functional capacity and productivity of these compositionally discrete pathogenic microbiota is paramount to dictating host immune responses and clinical disease severity. Indeed programs of metabolic productivity idiosyncratic to the predicted pathways encoded by bacteria present in distinct MCS were identified. In particular, 9- and 13-HODE, 9,10-DiHOME, and lysophosphatidylcholines (all significantly enriched in MCS1) increase leukocyte recruitment and pro-inflammatory cytokine secretion (102-105, 108-110). Prevention of 9,10-DiHOME formation via inhibition of soluble epoxide hydrolases attenuates disease in both chemical and genetic murine models of UC (140, 141). In addition to enrichment of leukocyte chemotactic metabolites, MCS1 patients also had high fecal concentrations of p-cresol sulfate, a known microbially derived metabolite (142), and putrescine, both of which can stimulate leukocyte oxidative burst (97, 98, 100, 101). Consistent with these observations, ophtalmate was also enriched in MCS1 patients, indicative of greater oxidative stress due to low or depleted levels of reactive oxygen species (ROS) quenching glutathione (95, 96). While the metabolome of high disease severity MCS1 indicate high oxidative stress, that of UC-MCS associated with lower disease severity (MCS2-4) exhibit increased capacity for ROS quenching due to enhanced γ-glutamyltransferase activity indicated by enrichment of γ-glutamyl amino acids (critical for maintaining glutathione levels) and high fecal concentrations of superoxide scavenging myo-inositol (113-116). Metabolic signatures indicative of immunosuppressive activity including anti-inflammatory dipeptides (such as alanyl-glutamine) and myo-inositol, metabolites which afford protection in animal models of colitis via decreased expression of pro-inflammatory cytokines and reduced leukocyte recruitment and activity (111, 112, 118, 119) were also characteristically enriched in MCS2-4 with lower disease severity. This suggests the unique metabolic productivity associated with each MCS is capable of governing host immune activity and resulting differences in UC presentation.

MCS-specific metabolic programs provide a multi-faceted mechanism by which gut microbiota compositional states relate to clinical disease severity. Support for which comes from our demonstration *in vitro*, via exposure of human DCs to filter-sterilized fecal water prior to co-culture with T-cells, that the most severely ill MCS1 patients induced the greatest degree of Th2 skew in CD4+ T-cells. This suggests distinct programs of luminal microbial productivity in the distal gut differentially influence CD4+ T-cell populations and cytokine productivity *in vitro,* and that the most severely ill patients exhibit CD4+ dysfunction consistent with that traditionally reported for UC patients (120-122). Though pathogen associated molecular patterns (PAMPS) are traditionally considered paramount to driving host immune responses to microbes, emerging data in the field of immunometabolism, indicates microbially derived metabolites are equally effective in driving immune cell phenotypes. For example, in addition to the immunomodulatory activity of microbially derived metabolites (such as short chain fatty acids and p-cresol sulfate) described above (24, 25, 42, 99-101), microbially derived metabolites of linoleic acid can suppress production of pro-inflammatory cytokines in mature DCs, demonstrate antioxidant characteristics, reduce allergic IgE production, regulate host Th1:Th2 ratios, and dampen production of PGE_2 and IL-12 in monocyte (143). Indeed our data suggests specific programs of microbial-derived metabolism in combination with an array of PAMPS presented by pathogenic bacteria and fungi in the distal gut of UC patients serve as effective drivers of immune dysfunction related to UC disease severity. Hence rationally designed strategies to re-engineer microbial community composition and productivity in the distal gut in a MCS-tailored manner, may prove a highly effective strategy for treatment of UC.

MATERIALS & METHODS

Participant Enrollment

This study was approved by the Committee on Human Research at the University of California, San Francisco (CHR # 10-03092). Physician diagnosed Ulcerative Colitis patients (age 18 to 60 years old) were recruited directly from the gastroenterology clinic at UCSF's Mount Zion Campus. A questionnaire was provided to each patient to assess clinical measures of disease severity [Simple Clinical Colitis Activity index (SCCA) (94), extra-colonic manifestations (arthritis, pyoderma gangrenosum, erythema nodosum, and uveitis), number of first- and second-degree relatives diagnosed with IBD, and duration of disease (years since UC diagnosis)]. Healthy volunteers (age 18 to 60 years old) were drawn from patients' families and by word of mouth. All participants were self-reported to be of either European or South Asian ethnicity. Additionally, all participants resided within a 70-mile radius of San Francisco, CA. Any participant experiencing pregnancy or breast feeding, severe concomitant disease involving the liver, heart, lungs or kidneys, or antibiotic treatment within the preceding 2 months were excluded from the study.

Fecal Sample Collection

Study participants were provided detailed instructions and necessary materials for fecal sample collection. Standardized fecal samples (first stool of the morning) were collect at home by defecating onto a sterile stool collection device (Cat. No. Protocult #120; Ability Building Center, MN) placed over a toilet seat and using a sterile collection cup with an attached sterile scoop (Cat. No. 80.734.311; Sarstedt, Germany). Following collection, fecal samples were placed in a pre-paid overnight mailer with a frozen ice pack (Cat. No. S-9902; ULINE, CA) and shipped overnight via USPS in accordance with federal regulations. Upon arrival, fecal sample were immediately stored at -80ºC.

Fecal DNA Isolation

DNA was extracted from individual fecal samples using a combination of bead beating and the commercially available QIAamp® DNA Stool Kit (Cat. No. 51504; QIAGEN, CA). Initially, 1.6mL of Buffer ASL was added to approximately 100mg of feces and bead beat for 30 s at 6.0 m/s in a FastPrep-24 instrument (Cat. No. 116004500; MP Biomedicals). Following bead beating, samples were incubated at 95ºC for 5 minutes to improve lysis efficiency of difficult to lyse microbes. The remainder of the DNA isolation was conducted using a QIAcube (Cat. No. 9001292; QIAGEN, CA) according to the QIAamp® DNA Stool Kit Protocol: Isolation of DNA from Stool for Pathogen Detection. Isolated DNA was stored at -80ºC. Blank extractions were included as negative controls to monitor for bacterial contamination.

Bacterial 16S rRNA Gene Profiling Using PhyloChip

Total DNA extracted from fecal samples was used as template for 16S rRNA gene amplification as previously described (72). PCR amplification was verified on a 1% TBE agarose gel then purified using the QIAquick Gel Extraction kit (Cat. No. 28704; QIAGEN, CA). A total of 500ng of purified PCR product per sample was then fragmented, biotin-labeled, and hybridized to the G3 16S rRNA PhyloChip (Affymetrix, CA) as previously described (73). Washing, staining, and scanning of arrays were conducted according to standard Affymetrix protocol (73). Background subtraction, detection, taxon quantification criteria and array normalization was performed as previously described (73). Stage 1 thresholds were adjusted, based on quantitative standards to the following: $rQ1 \geq 0.25$, $rQ2 \geq 0.50$, $rQ3 \geq 0.80$. All PhyloChip microarray data reported in this paper has been deposited in the Gene Expression Omnibus (GEO) database, www.ncbi.nlm.nih.gov/geo (accession no. GSE78724).

Bacterial 16S rRNA Gene Library Preparation

Bacterial 16S rRNA gene sequencing libraries were created as previously described (144). PCR amplification of the 16S rRNA gene was conducted in triplicate for each sample using barcoded primers targeting the V4 region (Supplemental Table S13) as previously described (144). Blank extractions were used as template for negative controls to monitor for 16S rRNA contamination. PCR reactions were performed in 25 µl reactions using 0.025 U Takara Hot Start ExTaq (Takara Mirus Bio Inc, Madison, WI), 1X Takara buffer with $MgCl_2$, 0.4 pmol $µl^{-1}$ of F515 and R806 primers, 0.56 mg ml^{-1} of bovine serum albumin (BSA; Roche Applied Science, Indianapolis, IN), 200 µM of dNTPs, and 10 ng of gDNA. Reactions were performed in triplicate under the following conditions: initial denaturation (98 °C for 2 min) followed by 30 cycles of 98 °C (20 sec), annealing at 50 °C (30 sec), extension at 72 °C (45 sec) and a final extension at 72 °C for 10 min. Following PCR, triplicates were pooled and 16s rRNA amplicon concentrations were determined via gel electrophoresis quantitation. 16S rRNA sequence library was created by pooling all PCR amplicons in equimolar concentrations to a final volume of 75uL. To remove background, the 16S rRNA sequence library was run on a 2% agarose gel and the 16S amplicon (~380bp) was purified using the QIAquick Gel Extraction Kit (Cat. No. 28704; QIAGEN, CA).

Fungal ITS2 Library Preparation

Fungal internal transcribed spacer 2 (ITS2) sequencing libraries were created using similar methods to those used for the 16S rRNA library. PCR amplification of the ITS2 region was conducted in triplicate for each sample using barcoded primers (Supplemental Table S14). PCR reactions were performed in 25 µl reaction with 1X Takara buffer (Takara Mirus Bio), 200 nM of each primer, 200 µM dNTPs, 2.75 mM of $MgCl_2$, 0.56 mg ml^{-1} of BSA (Roche Applied Science), 0.025 U Takara Hot Start ExTaq and 50 ng of gDNA. Reactions were conducted under the following conditions: initial denaturation (94 °C for 5 min) followed by 30 cycles of 94 °C (30 sec), annealing at 54 °C (30 sec), extension at 72 °C (30 sec) and a final extension at 72

°C for 7 min. Following PCR, triplicates were pooled and purified using the Agencourt AMPure XP - PCR Purification Kit and associated protocol (Cat. No. A63880, Beckman Coulter). Samples were quantified using the KAPA SYBR FAST qPCR Kit (Cat. No. KK4601, KAPA Biosystems) as recommended by the manufacturers. All purifed samples were then pooled in equimolar concentrations based individual sample ITS2 quantification to a final volume of 75uL.

16S and ITS2 Library Sequencing

Purified sequencing libraries were analyzed using a Bioanalyzer (Aligent), quantified using the Qubit HS dsDNA kit (Invitrogen), and diluted to 2 nM. Diluted sequence libraries were then denatured, diluted to 5.88pM, and combined with denatured 12.5pM PhiX spike-in to final concentration of 5pM. Prepared sequencing libraries were then loaded onto the Illumina MiSeq cartridge (Cat. No. MS-102-3001, Illumina) and sequenced (514 cycles, Read 1: 251 cycles, Index Read: 12 cycles, Read 2: 251 cycles) using a MiSeq platform and MiSeq Control Software v2.2.0 according to the manufacturer's instructions (Illumina). All sequence data related to this study is available in the NCBI Sequence Read Archive (SRA), http://www.ncbi.nlm.nih.gov/sra (accession no. PRJNA313074).

Bacterial 16S rRNA Sequence Processing

Following paired-end sequencing, paired sequences were assembled using FLASH v1.2.7 with a minimum overlap set at 15bp. Assembled reads were de-multiplexed by barcode and filtered for low quality (Q-score < 30) using QIIME 1.8 (145). If the Q-score three consecutive bases were <30, the read was truncated before the low-quality bases. The resulting read was retained in the dataset if it was at least 75% of the original length. Operational taxonomic units (OTUs) were picked at 97% sequence identity using uclust against the GreenGenes 13_8 database (146) (147), retaining OTUs containing >1 sequence read. Reads that failed to hit the reference sequence collection were retained and clustered *de novo*.

Sequences were aligned using PyNAST and taxonomy was assigned using uclust and the GreenGenes 13_8 database (148) (146) (147). PyNAST-aligned sequences were chimera checked using ChimeraSlayer (149), removing putative chimeras and representative sequences that failed PyNAST alignment. A phylogenetic tree was built using FastTree (150). To normalize variation in read depth across samples, data were rarefied to the minimum read depth of 49,518 sequences per sample for bacteria. To ensure that a truly representative community of each sample was used for analysis, sequence sub-sampling at the defined depth was bootstrapped 100 times. The representative community composition for each sample was defined as that which exhibited the minimum average Canberra distance to all other OTU vectors generated from all sub-samplings for that particular sample.

Fungal ITS2 Sequence Processing

Following paired-end sequencing, paired sequences were assembled using FLASH v1.2.7 with a minimum overlap of 25 bp and a maximum overlap of 290bp. Assembled reads were de-multiplexed by barcode using QIIME 1.8 (145). Assembled reads containing >2 expected errors, as determined by usearch (146), were removed. Singleton reads were removed and OTUs of 97% sequence similarity were generated *de novo* using usearch8.0 (146). The 8_1_2015 UNITE ITS fungal sequence database and usearch8.0 was used to remove potentially chimeric sequences (151) (146). The ITSx software package was then used to extract the predicted ITS2 region from the reference sequence of non-chimeric OTUs, filtering out OTUs predicted to lack a true ITS2 region in the process (152). Taxonomy was then assigned to non-chimeric, ITS2 extracted OTUs using Bayesian classification with a confidence cut-off of 0.8 in QIIME according to the 8_1_2015 UNITE ITS fungal sequence database (145) (151). OTUs responsible for less that 0.001% of the total sequence reads were removed. To normalize variation in read depth across samples, data were rarefied to the minimum read depth of 6,653 sequences per sample for bacteria. To ensure that a truly representative community of each sample was used for analysis, sequence sub-sampling at the defined depth was bootstrapped 100 times. The representative community composition for each sample was defined as that which exhibited the minimum average Canberra distance to all other OTU vectors generated from all sub-samplings for that particular sample.

Predicted community metagenome analyses

Phylogenetic Investigation of Communities by Reconstruction of Unobserved States (PICRUSt; http://picrust.github.io/picrust/), a bioinformatics software package used to predict functional metagenomes from a marker gene survey (such as 16S rRNA gene), was used to generate *in silico* bacterial metagenomes for data generated in this study (52). First, the biom-formatted bacterial OTU table previously generated from the processed 16S rRNA gene MiSeq data was filtered to contain only closed-reference OTUs [i.e. OTUs present in the GreenGenes 16S rRNA 13_8 database (147)]. The closed-reference OTU table was then used to generate predicted metagenomes according to the PICRUSt metagenome prediction tutorial (http://picrust.github.io/picrust/tutorials/metagenome_prediction.html - metagenome-prediction-tutorial). Briefly, OTU abundance was first normalized according to known or predicted 16s copy number. Following 16s copy number normalization, this normalized OTU table was then used to predicted KEGG Ortholog (KO) abundances for each sample, which were further collapsed into KEGG Pathways (http://www.genome.jp/kegg/pathway.html).

Metabolome Profiling

To profile fecal metabolites, >200mg of frozen stool from each sample was shipped overnight on dry ice to Metabolon (Metabolon, NC). Also included were several technical replicate samples created from a homogeneous pool containing a small amount of all study sample. Upon receipt, samples were inventoried, and immediately stored at -80ºC. At the time of analysis, samples were extracted and prepared for analysis using Metabolon’s standard solvent extraction method (http://www.metabolon.com/). The extracted samples were split into equal parts for analysis on the GC/MS and Q-Exactive accurate mass LC/MS platforms.

Sample Preparation: The sample preparation process was carried out using the automated MicroLab STAR® system from Hamilton Company. Recovery standards were added prior to the first step in the extraction process for QC purposes. Sample preparation was conducted using a proprietary series of organic and aqueous extractions to remove the protein fraction while allowing maximum recovery of small molecules. The resulting extract was divided into two fractions; one for analysis by LC/MS and one for analysis by GC/MS. Samples were placed briefly on a TurboVap® (Zymark) to remove the organic solvent. Each sample was then frozen and dried under vacuum. Samples were then prepared for the appropriate instrument, either LC/MS or GC/MS.

QA/QC: For QA/QC purposes, a number of additional samples were included with each day's analysis. Furthermore, a selection of QC compounds was added to every sample, including those under test. These compounds were chosen so as not to interfere with the measurement of the endogenous compounds. Tables 1 and 2 describe the QC samples and compounds. These QC samples are primarily used to evaluate the process control for each study as well as aiding in the data curation.

Table 1: Description of Metabolon QC Samples

Type	Description	Purpose
MTRX	Large pool of human plasma maintained by Metabolon that has been characterized extensively.	Assure that all aspects of Metabolon process are operating within specifications.
CMTRX	Pool created by taking a small aliquot from every customer sample.	Assess the effect of a non-plasma matrix on the Metabolon process and distinguish biological variability from process variability.
PRCS	Aliquot of ultra-pure water	Process Blank used to assess the contribution to compound signals from the process.
SOLV	Aliquot of solvents used in extraction.	Solvent blank used to segregate contamination sources in the extraction.

Table 2: Metabolon QC Standards

Type	Description	Purpose
DS	Derivatization Standard	Assess variability of derivatization for GC/MS samples.
IS	Internal Standard	Assess variability and performance of instrument.
RS	Recovery Standard	Assess variability and verify performance of extraction and instrumentation.

Ultrahigh Performance Liquid Chromatography/Mass Spectroscopy (UPLC/MS/MS): The LC/MS portion of the platform was based on a Waters ACQUITY ultra-performance liquid chromatography (UPLC) and a Thermo Scientific Q-Exactive high resolution/accurate mass spectrometer interfaced with a heated electrospray ionization (HESI-II) source and Orbitrap mass analyzer operated at 35,000 mass resolution. The sample extract was dried then reconstituted in acidic or basic LC-compatible solvents, each of which contained 8 or more injection standards at fixed concentrations to ensure injection and chromatographic consistency. One aliquot was analyzed using acidic positive ion optimized conditions and the other using basic negative ion optimized conditions in two independent injections using separate dedicated columns (Waters UPLC BEH C18-2.1×100 mm, 1.7 µm). Extracts reconstituted in acidic conditions were gradient eluted using water and methanol containing 0.1% formic acid, while the basic extracts, which also used water/methanol, contained 6.5mM Ammonium Bicarbonate. The MS analysis alternated between MS and data-dependent MS2 scans using dynamic exclusion, and the scan range was from 80-1000 m/z. Raw data files are archived and extracted as described below.

Gas chromatography/Mass Spectrometry (GC/MS): The samples destined for GC/MS analysis were re-dried under vacuum desiccation for a minimum of 24 hours prior to being derivatized under dried nitrogen using bistrimethyl-silyl-triflouroacetamide (BSTFA). The GC column was 5% phenyl/ 95% dimethyl polysiloxane fused silica column and the temperature ramp was from 40° to 300° C in a 16 minute period. Samples were analyzed on a Thermo-Finnigan Trace DSQ fast-scanning single-quadrupole mass spectrometer using electron impact ionization. The instrument was tuned and calibrated for mass resolution and mass accuracy on a daily basis. The information output from the raw data files was automatically extracted as discussed below.

Data Extraction and Compound Identification: Raw data was extracted, peak-identified and QC processed using Metabolon's hardware and software. Compounds were identified by comparison to library entries of purified standards or recurrent unknown entities. Metabolon maintains a library based on authenticated standards containing the retention time/index (RI), mass to charge ratio (m/z), and chromatographic data (including MS/MS spectral data) on all molecules present in the library. Furthermore, biochemical identifications are based on three criteria: retention index within a narrow RI window of the proposed identification, nominal mass match to the library +/- 0.4 amu, and the MS/MS forward and reverse scores between the experimental data and authentic standards. The MS/MS scores are based on a comparison of the ions present in the experimental spectrum to the ions present in the library spectrum.

Normalization: For studies spanning multiple days, a data normalization step was performed to correct variation resulting from instrument inter-day tuning differences. Essentially, each compound was corrected in run-day blocks by registering the medians to equal one (1.00) and normalizing each data point proportionately. For studies that did not require more than one day of analysis, no normalization was necessary.

Fecal Water Preparation

Fecal samples were diluted in sterile 37°C PBS containing 20% FBS and 2mM EDTA to a final concentration of 1g/mL. Diluted fecal samples were then vortex for 1 minutes and incubated at 37°C for 10 minutes. Following incubation, samples were centrifuged at ~21,000g for 10 minutes at room temperature to remove insoluble material. Supernatants were then filtered through a 0.2μm nylon filter to obtain sterile fecal water. Sterile fecal water solutions were stored at -20ºC.

In vitro dendritic cells fecal water exposure and co-culture with autologous T-cells

Peripheral blood samples were obtained from anonymous healthy human donors (Blood Centers of the Pacific, San Francisco, CA). Peripheral blood mononuclear cells (PBMCs) were isolated by Ficoll-Hypaque gradient centrifugation (Cat. No. Histopaque-10771; Sigma-Aldrich). Dendritic cells (DCs) were purified from isolated PBMCs using the EasySep™ Human Pan-DC Pre-Enrichment Kit (Cat. No. 19251; STEMCELL Technologies, Canada) and cultured in 96-well plates (0.5 x 10^6 cells/ml) in fresh R10 media: RPMI 1640 (Cat. No. 11875; Thermo-Fisher Scientific) supplemented with 10% heat-inactivated FCS (Cat. No. 9871-5244; USA Scientific), 100 U/ml penicillin-streptomycin (Cat. No. 10378016; Life Technologies, CA), 10 ng/ml GM-CSF (Cat. No. 15-GM-010; R&D Systems, MN), and 20 ng/ml IL-4 (Cat. No. 204-IL-010; R&D Systems). Prepared sterile fecal water was added to DC culture at a 1/20 dilution. After a 24 hour incubation, cells were stimulated with 10 ng/ml TNF-α (Cat. No. 300-01A; PeproTech, NJ), 10 ng/ml IL-1β (Cat. No. 200-01B; PeproTech), 10 ng/ml IL-6 (Cat. No. AF-200-06; PeproTech), and 1μM PGE2 (Cat. No. 72194; STEMCELL Technologies) and incubated for an additional 24 hours to induce DC maturation. T-cells were purified from autologous, monocyte-depleted PBMCs by negative selection using the Human T-Cell Enrichment Column (Cat. No. HTCC-2000; R&D Systems) and were subsequently cultured in TexMACS Medium (Cat. Not. 130-097-196; Miltenyi Biotec, Germany). Following DC stimulation, DCs were harvested, washed, and co-cultured with autologous T-cells at a ratio of 1/10 in the presence of 1ug/ml soluble anti-CD28 (Cat. No. 555725; BD Biosciences, CA) and 1 μg/ml anti-CD49d (Cat. No. 555501; BD Biosciences) for 5 days, replenishing the media every 2 days. This assay was repeated four times using PBMCs obtained from distinct donors to ensure observations were independent of PBMC source.

Flow Cytometry

To assess cytokine production, the co-cultures were stimulated with Phorbol Myristate Acetate-Ionomycin (Cat. No. 356150010; Fisher Scientific) and GolgiPlug (Cat. No. 555029; BD Biosciences) for 16 hours. Cells were harvested and single-cell suspensions were stained in two separate antibody panels to assess phenotype. Panel 1: anti-CD3 (Cat. No. 557917; BD Biosciences), anti-CD4 (Cat. No. 563028; BD Biosciences), anti-CD8a (Cat. No. 563821; BioLegend), anti-CD25 (Cat. No. 557741; BD Biosciences), anti-FoxP3 (Cat. No. 14-4776-80; eBioscience), and anti-IL10 (Cat. No. 130-096-043; Miltenyi Biotec). Panel 2: anti-CD3 (Cat. No. 557917; BD Biosciences), anti-CD4 (Cat. No. 563028; BD Biosciences), anti-CD8a (Cat. No. 563821; BioLegend), anti-CD69 (Cat. No. 560737; BD Biosciences), anti-INFγ (Cat. No. 560371; BD Biosciences), anti-IL4 (Cat. No. 130-091-647; Miltenyi Biotec), anti-IL17A (Cat. No. 17-7179-42; eBioscience), and anti-IL22 (Cat. No. 25-7229-42; eBioscience). Cells were permeabilized by either Cytofix/Cytoperm™(Cat. No. 554714; BD Bioscience) or Fixation/ Permeabilization (Cat. No. 00-5523-00; Affymatrix eBioscience).

Upon staining, live T-cells were gated as CD3$^+$ CD4$^+$ or CD3$^+$ CD8$^+$ cells. Activated T-cells were surface stained CD69hi. Among the CD4$^+$ T-cell population, subpopulations were defined as Th1: IFNγ$^+$, Th2: IL-4$^+$, Th17: IL-17A$^+$, Th22: IL17A$^-$ and IL-22$^+$, and Treg: CD25hi and FoxP3hi. CD8$^+$ T-cells subpopulations were defined as Tc1: IFNγ$^+$, Tc2: IL-4$^+$, and Tc17: IL-17A$^+$. Stained cells were assayed via flow cytometry on a BD LSR II (BD Biosciences).

Cytometric Bead Array

Prior to addition of PMA/Gplug, 100 uL of cell-free supernatant was removed from each co-culture and centrifuged for 1 minute at 3000 rpm. Cytokine secretion was measured using a cytometric bead array (BD Biosciences) and the concentration of IL-4, IL-5, IL-13, and were determined according to the manufacturer’s guidelines. Data was acquired by flow cytometry on a BD LSR II (BD Biosciences) and data analysis was performed using the proprietary FCAP Array analysis software (BD Biosciences).

Statistical analysis

Microbial, Metagenomic, and Metabolomic Analysis: Analysis was performed using QIIME v1.8.0 and the R statistical environment (145, 153). Shannon's Diversity and Faith's Phylogenetic Diversity were calculated using QIIME v 1.8.0 and two-tailed t-tests were performed to identify significant between group differences (e.g. UC vs. Healthy) (145). Weighted UniFrac, Canberra, and Bray-Curtis distance matrices were generated using QIIME v 1.8.0 and visualized via NMDS in the R statistical environment using the *vegan* package (154, 155). For PhyloChip data, fluorescent intensities were log-normalized prior to calculating Canberra distances. Permutational multivariate analysis of variance (PERMANOVA) using calculated distance matrices was used to determine relationships between existing metadata (i.e. Health Status or Ethnicity) and bacterial, fungal, metagenome, or metabolome composition using the *adonis* function found in *vegan* (155). Hierarchical cluster analysis combined with multi-scale, bootstrap resampling was performed using the *pvclust* package in R with 1000 bootstrap replications (156). Correlation between distances matrices was calculated using the *mantel* function found in *vegan* (155). To identify significantly enriched or depleted bacterial OTUs, fungal OTUs, and KEGG pathways between relevant sample groups (e.g. UC vs. Healthy), the three-model approach described by Romero *et al.* was applied (157). Briefly, three linear mixed-effect regression models (negative binomial, zero-inflated negative bionomial, and Poisson) were independently fit to each observation (i.e. OTU or KEGG pathway) and the model with lowest Akaike Information Criterion (AIC) was retained. P-values were computed for only the best-fit models (i.e. those that minimized AIC). To account for false discovery, q-values were calculated based on the computed p-values. For PhyloChip data, significantly enriched or depleted OTUs were determined by applying a two-tailed t-test to log-normalized fluorescent intensities. To identify significantly enriched or depleted fecal metabolites, log-normalized relative concentrations were compared using a Welch's t-test.

Comparison of Clinical Measures of Disease Severity: Clinical measures of disease severity (i.e. SCCA, number of extra-colonic manifestations, number of diagnosed first- and second-degree relatives, and years since diagnosis were compared between UC-MCS by a Kruskal-Wallis Test followed by pairwise tw-tailed Dun's Test.

Analysis of T-cell Subsets: Because the T-cell assay described above was repeated four separate times using PBMCs from four different PBMC donors, a linear mixed effects model was applied using the *lme4* package in R to identify significant differences in the abundance of induced T-cell subpopulations based on sample group (i.e. UC-MCS) while accounting for potential variation introduced due to PBMC source (i.e. donor) (158). The following linear mixed effects models were applied to identify changes due to health status (Healthy vs. UC) and UC-MCS (Healthy vs. MCS1, MCS2, MCS3, MCS4) respectively:

$$Y \sim \beta(\text{EXP\_GROUP}) + \mu(\text{DONOR}) + \mu(\text{SAMPLE}) + \varepsilon$$

$$Y \sim \beta(\text{MCS}) + \mu(\text{DONOR}) + \mu(\text{SAMPLE}) + \varepsilon$$

Where Y = a measured, dependent variable such as Th1 abundance, EXP_GROUP = health status (Healthy or UC), MCS = microbial community state (Healthy, MCS1, MCS2, MCS3, or MCS4), DONOR = PBMC donor source (Donor #1 to #4), and SAMPLE = fecal sample study participant.

SUPPLEMENTARY FIGURES & TABLES

Figure S1.

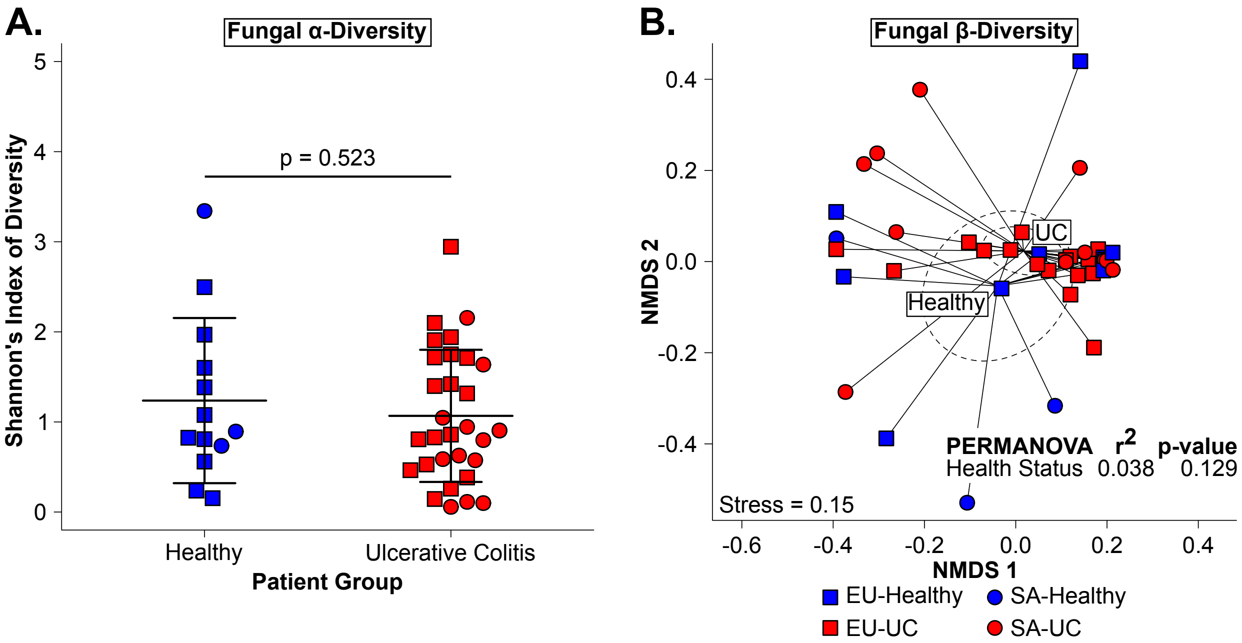

Figure S1. Comparison of the Healthy (n = 13) and UC-associated (n = 30) fecal fungal microbiota. (A) Fungal α-diversity. Horizontal bars represent mean +/- standard deviation. P-values obtained by two-tailed T-test. **(B)** Fungal community composition represented by NMDS of pairwise Bray-Curtis distances. Dashed ellipses represent the 95% confidence interval for the average coordinates of each participant stratification group as calculated by *envfit*. Each dot/square represents a single fecal sample obtained from a single donor: EU-Healthy (square, blue fill), SA-Healthy (circle, blue fill), EU-UC (square, red fill), and SA-UC (circle, red fill).

Figure S2.

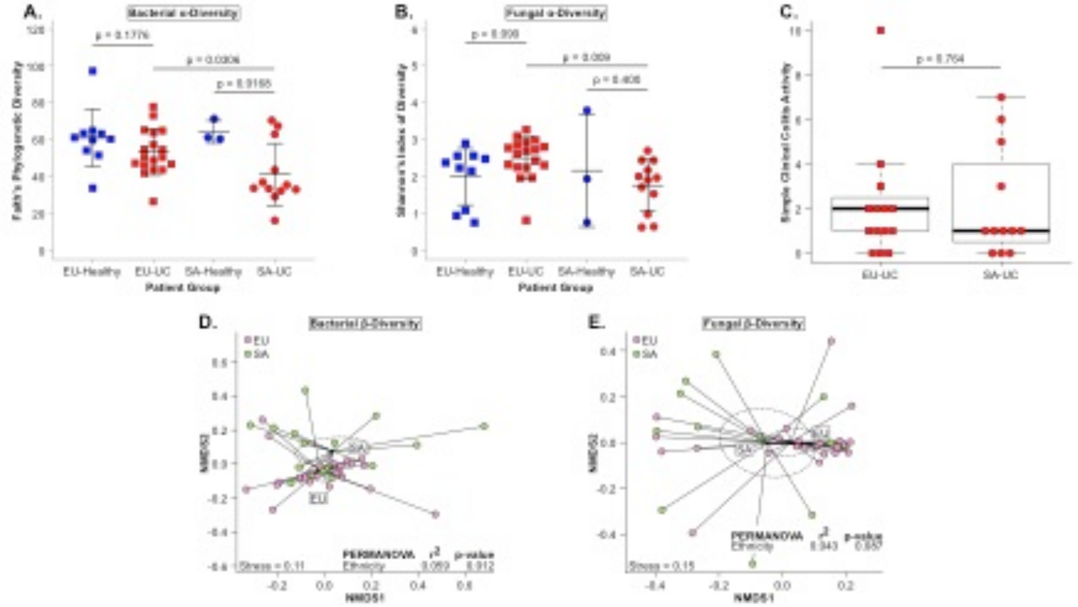

Figure S2. Comparison of the Healthy (n = 10 EU, 3 SA) and UC-associated (n = 18 EU, 12 SA) fecal microbial diversity taking participants' ethnicity into account. (A) Bacterial α-diversity. **(B)** Fungal α-diversity. Horizontal bars represent mean +/- standard deviation. P-values obtained by two-tailed T-test. **(C)** Simple Clinical Colitis Activity of UC patients stratified by ethnicity (n = 14 EU-UC, 12 SA-UC). P-value obtained by two-tailed Rank-Sum Test. **(D)** Bacterial community composition of all participants stratified by ethnicity (n = 28 EU, 15 SA) represented by NMDS of pairwise Weighted UniFrac distance. **(E)** Fungal community composition of all participants stratified by ethnicity (n = 28 EU, 15 SA) represented by NMDS of pairwise Bray-Curtis distance. Dashed ellipses represent the 95% confidence interval for the average coordinates of each participant stratification group as calculated by *envfit*. Each dot/square represents a single fecal sample obtained from a single donor.

Figure S3.

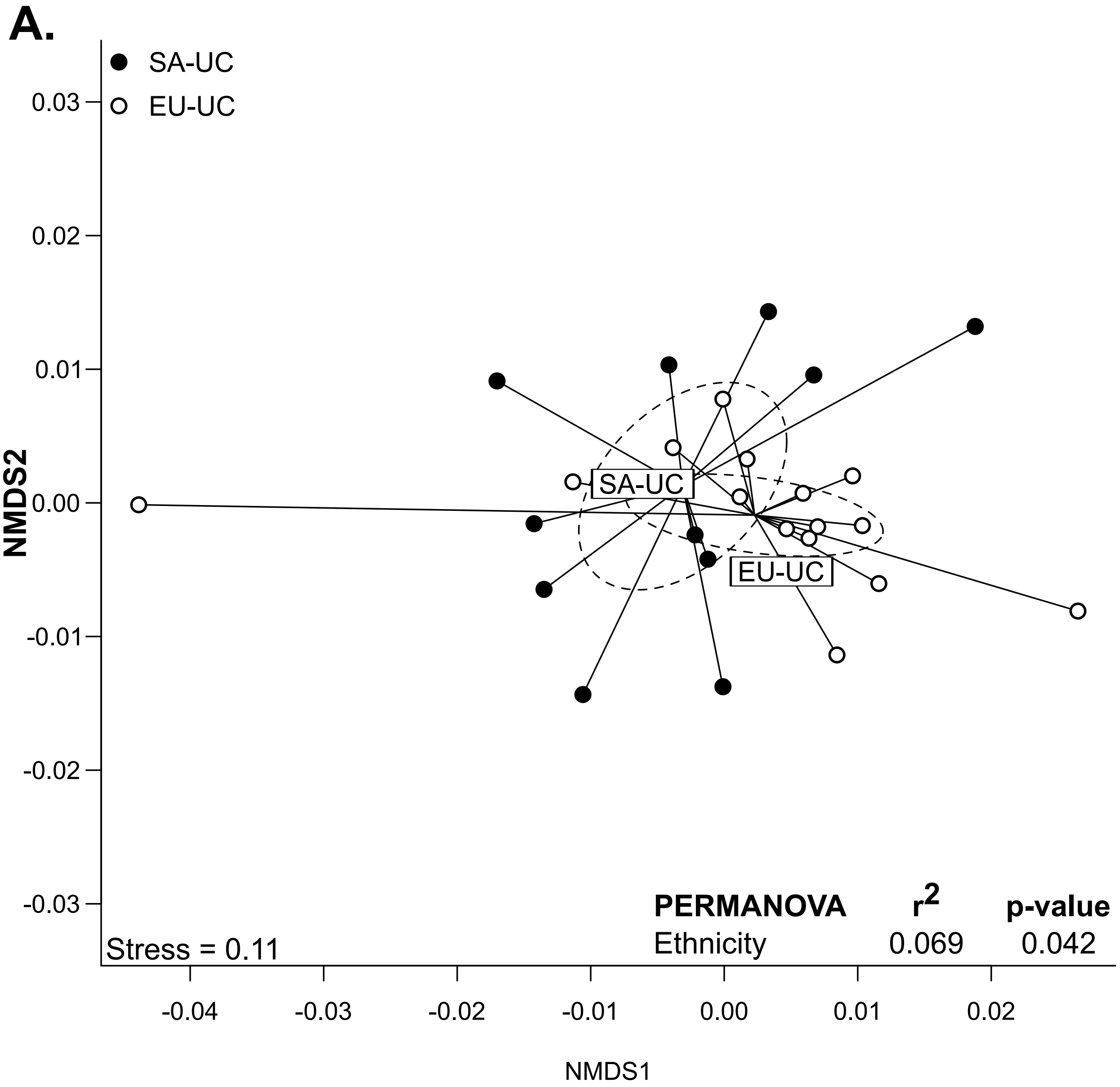

Figure S3. PhyloChip profiled bacterial community composition of UC-patients stratified by ethnicity (n = 15 EU-UC, 11 SA-UC) represented by NMDS of pairwise Canberra distance. Dashed ellipses represent the 95% confidence interval for the average community coordinates of each participant stratification group as calculated by *envfit*. Each dot/square represents a single fecal sample obtained from a single donor.

Figure S4.

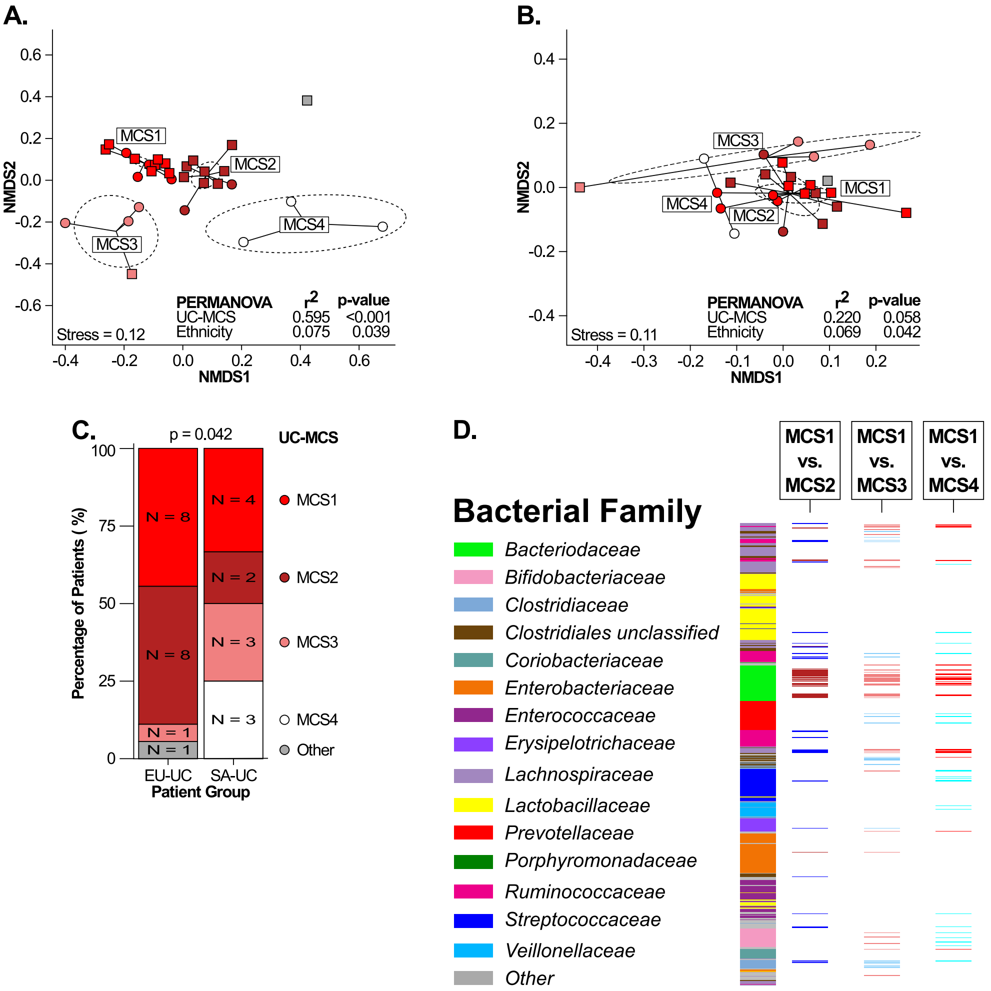

Figure S4. Bacterial community composition of UC-patients stratified by UC-MCS. (A) NMDS of pairwise Weighted UniFrac distances for 16S rRNA profiles obtained via Illumina MiSeq (n = 12 MCS1, 10 MCS2, 4 MCS3, 3 MCS4, 1 Other). **(B)** NMDS of pairwise Canberra distances for 16S rRNA profiles obtained via PhyloChip (n = 10 MCS1, 8 MCS2, 4 MCS3, 2 MCS4, 1 Other). Dashed ellipses represent the 95% confidence interval for the average community coordinates of each participant stratification group as calculated by *envfit*. Each dot/square represents a single fecal sample obtained from a single donor. **(C)** Distribution of UC-MCS according to patient ethnicity. P-value obtained by Fisher's Exact Test. **(D)** Bacterial OTUs significantly enriched (red shade) or depleted (blue shade) in MCS1 vs. MCS2, -3, or -4 respectively (p-value < 0.05, see materials & methods).

Figure S5.

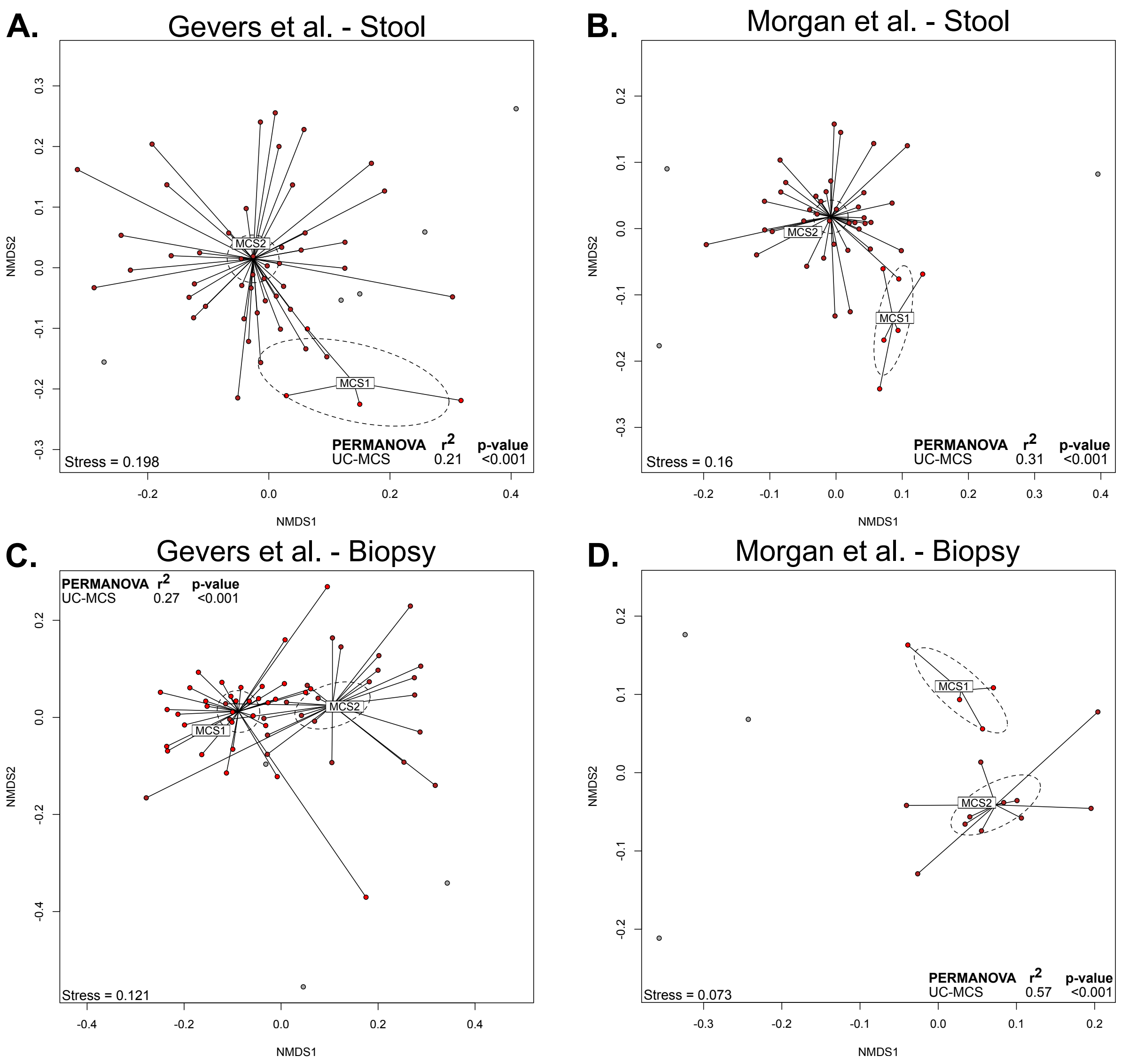

Figure S5. Identification of predominantly EU UC-MCS (MCS1 and -2) in two publicly available datasets. Bacterial community composition of UC-patients stratified by UC-MCS represented by NMDS of pairwise Weighted UniFrac distances. **(A)** Gevers *et al.* - Stool Samples (n = 56). **(B)** Morgan *et al.* - Stool Samples (n = 47). **(C)** Gevers *et al.* - Biopsies (n = 60). **(D)** Morgan *et al.* - Biopsies (n = 18). Dashed ellipses represent the 95% confidence interval for the average community coordinates of each participant stratification group as calculated by *envfit*. Each dot/square represents a single fecal sample obtained from a single donor.

Figure S6.

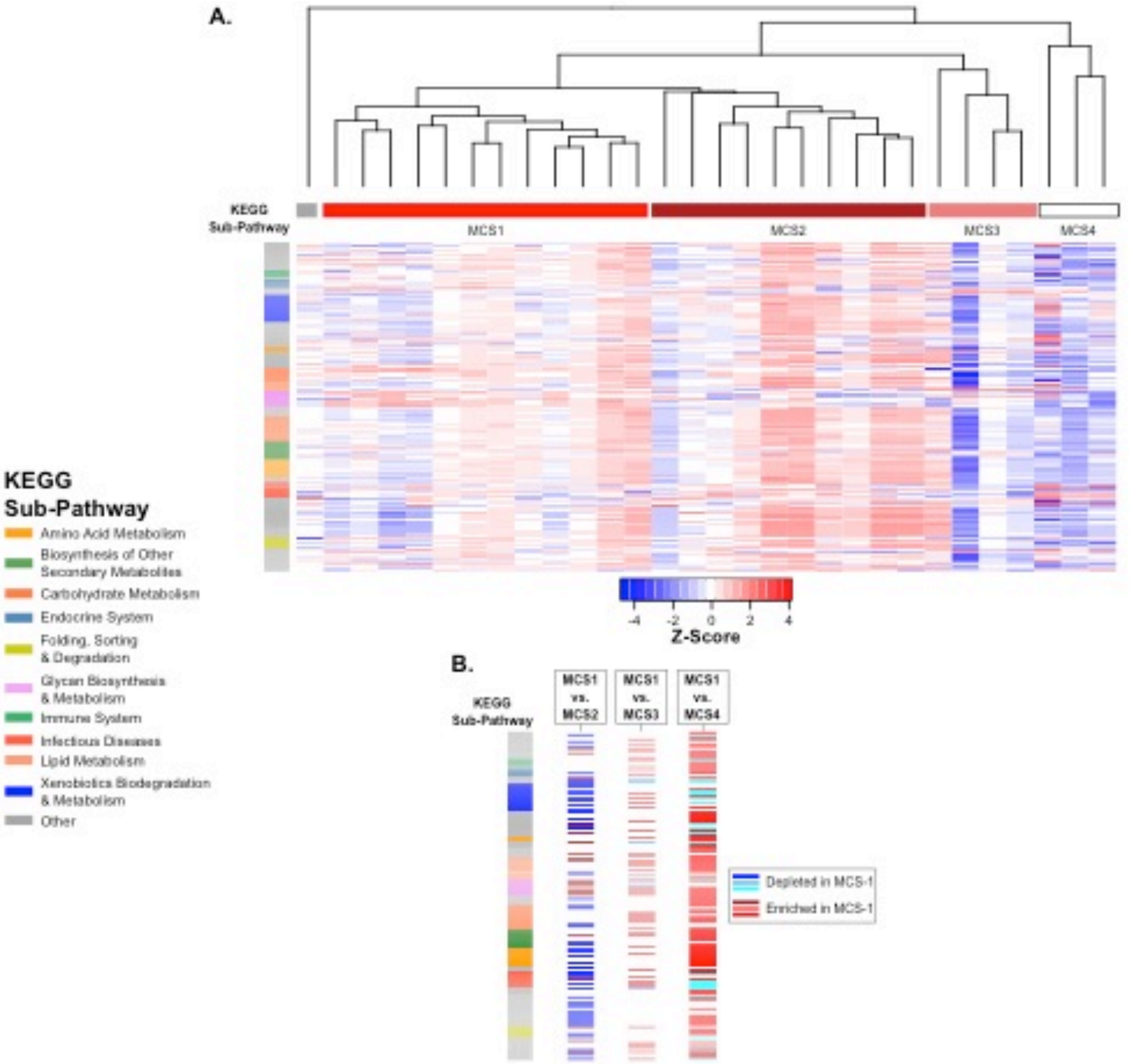

Figure S6. (A) Heatmap of differentially enriched KEGG pathways across UC-MCS. Depicted KEGG pathways were initially identified by Kruskal-Wallis test comparing distribution amongst UC-MCS (q-value < 0.0006). Column order is consistent with Fig. 2. Rows are order alphabetically by Super-pathway, Sub-pathway, and pathway. For visualization, read counts were normalized [log2(x+1)] and scaled by row. **(B)** KEGG pathways significantly enriched (red shade) or depleted (blue shade) in MCS1 vs. MCS2, -3, or -4 respectively (p-value < 0.05, see materials & methods).

Figure S7.

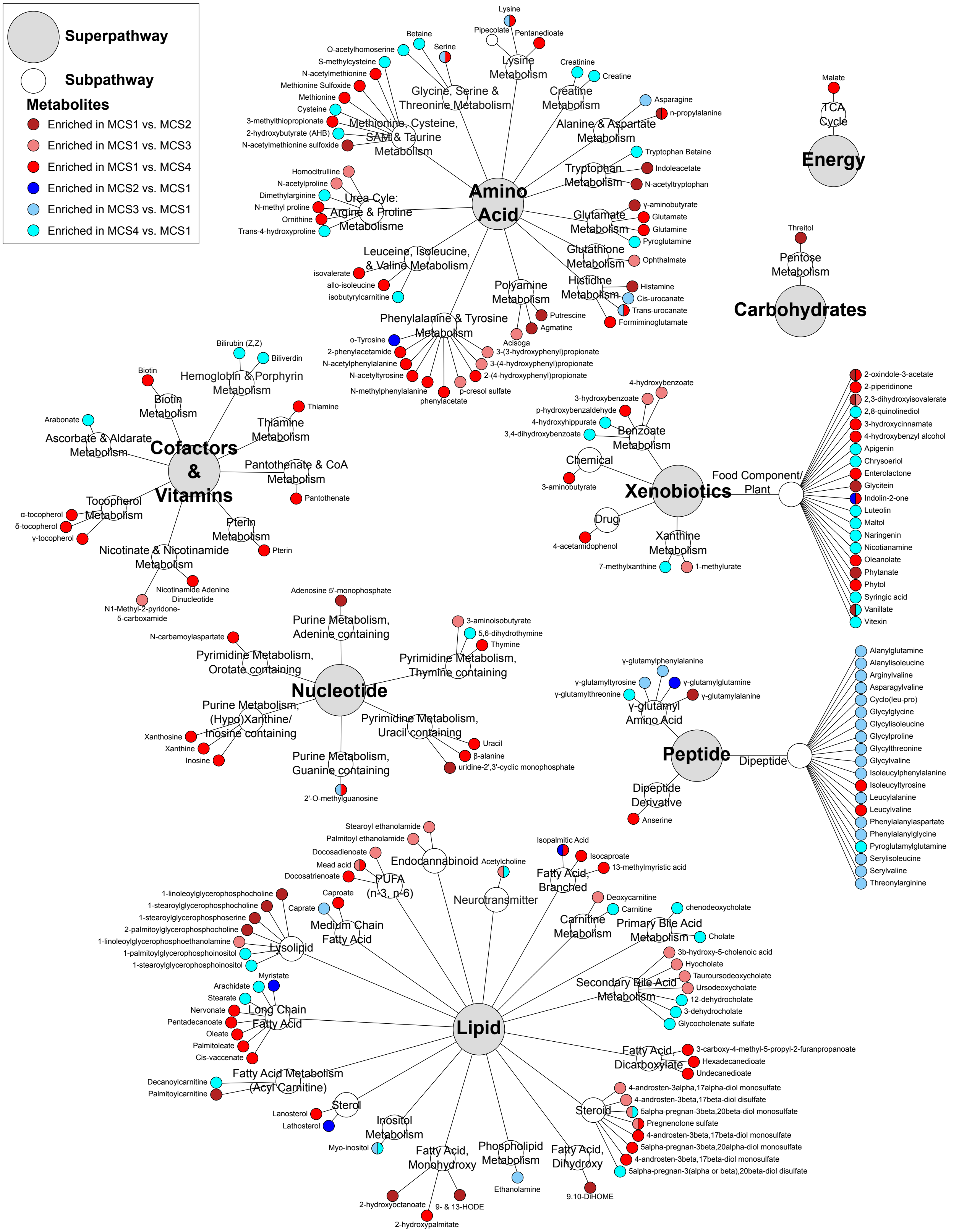
Superpathway
Subpathway
Metabolites
Enriched in MCS1 vs. MCS2
Enriched in MCS1 vs. MCS3
Enriched in MCS1 vs. MCS4
Enriched in MCS2 vs. MCS1
Enriched in MCS3 vs. MCS1
Enriched in MCS4 vs. MCS1
Amino Acid
Lysine
Pipecolate
Pentanedioate
Lysine Metabolism
Betaine
Serine
O-acetylhomoserine
Glycine, Serine & Threonine Metabolism
S-methylcysteine
N-acetylmethionine
Methionine Sulfoxide
Methionine
Cysteine
3-methylthiopropionate
2-hydroxybutyrate (AHB)
N-acetylmethionine sulfoxide
Methionine, Cysteine, SAM & Taurine Metabolism
Creatinine
Creatine
Creatine Metabolism
Asparagine
n-propylalanine
Alanine & Aspartate Metabolism
Tryptophan Betaine
Indoleacetate
N-acetyltryptophan
Tryptophan Metabolism
Homocitrulline
N-acetylproline
Dimethylarginine
N-methyl proline
Ornithine
Trans-4-hydroxyproline
Urea Cyle: Argine & Proline Metabolisme
γ-aminobutyrate
Glutamate
Glutamine
Pyroglutamine
Glutamate Metabolism
Ophthalmate
Glutathione Metabolism
Leuceine, Isoleucine, & Valine Metabolism
isovalerate
allo-isoleucine
isobutyrylcarnitine
Histamine
Cis-urocanate
Trans-urocanate
Formiminoglutamate
Histidine Metabolism
Polyamine Metabolism
Putrescine
Agmatine
Acisoga
Phenylalanine & Tyrosine Metabolism
o-Tyrosine
2-phenylacetamide
N-acetylphenylalanine
N-acetyltyrosine
N-methylphenylalanine
phenylacetate
p-cresol sulfate
3-(3-hydroxyphenyl)propionate
3-(4-hydroxyphenyl)propionate
2-(4-hydroxyphenyl)propionate
Malate
TCA Cycle
Energy
Threitol
Pentose Metabolism
Carbohydrates
Cofactors & Vitamins
Bilirubin (Z,Z)
Biliverdin
Hemoglobin & Porphyrin Metabolism
Biotin
Biotin Metabolism
Thiamine
Thiamine Metabolism
Arabonate
Ascorbate & Aldarate Metabolism
Pantothenate & CoA Metabolism
Pantothenate
α-tocopherol
δ-tocopherol
γ-tocopherol
Tocopherol Metabolism
Pterin Metabolism
Pterin
Nicotinate & Nicotinamide Metabolism
Nicotinamide Adenine Dinucleotide
N1-Methyl-2-pyridone-5-carboxamide
Xenobiotics
4-hydroxybenzoate
3-hydroxybenzoate
p-hydroxybenzaldehyde
4-hydroxyhippurate
3,4-dihydroxybenzoate
Benzoate Metabolism
Chemical
3-aminobutyrate
Drug
4-acetamidophenol
Xanthine Metabolism
7-methylxanthine
1-methylurate
Food Component/ Plant
2-oxindole-3-acetate
2-piperidinone
2,3-dihydroxyisovalerate
2,8-quinolinediol
3-hydroxycinnamate
4-hydroxybenzyl alcohol
Apigenin
Chrysoeriol
Enterolactone
Glycitein
Indolin-2-one
Luteolin
Maltol
Naringenin
Nicotianamine
Oleanolate
Phytanate
Phytol
Syringic acid
Vanillate
Vitexin
Nucleotide
Adenosine 5'-monophosphate
Purine Metabolism, Adenine containing
N-carbamoylaspartate
Pyrimidine Metabolism, Orotate containing
3-aminoisobutyrate
5,6-dihydrothymine
Thymine
Pyrimidine Metabolism, Thymine containing
Purine Metabolism, (Hypo)Xanthine/ Inosine containing
Xanthosine
Xanthine
Inosine
Pyrimidine Metabolism, Uracil containing
Uracil
β-alanine
uridine-2',3'-cyclic monophosphate
Purine Metabolism, Guanine containing
2'-O-methylguanosine
Peptide
γ-glutamylphenylalanine
γ-glutamyltyrosine
γ-glutamylglutamine
γ-glutamylthreonine
γ-glutamylalanine
γ-glutamyl Amino Acid
Dipeptide Derivative
Anserine
Dipeptide
Alanylglutamine
Alanylisoleucine
Arginylvaline
Asparagylvaline
Cyclo(leu-pro)
Glycylglycine
Glycylisoleucine
Glycylproline
Glycylthreonine
Glycylvaline
Isoleucylphenylalanine
Isoleucyltyrosine
Leucylalanine
Leucylvaline
Phenylalanylaspartate
Phenylalanylglycine
Pyroglutamylglutamine
Serylisoleucine
Serylvaline
Threonylarginine
Lipid
Stearoyl ethanolamide
Palmitoyl ethanolamide
Endocannabinoid
Docosadienoate
Mead acid
Docosatrienoate
PUFA (n-3, n-6)
Acetylcholine
Neurotransmitter
Isopalmitic Acid
Isocaproate
13-methylmyristic acid
Fatty Acid, Branched
1-linoleoylglycerophosphocholine
1-stearoylglycerophosphocholine
1-stearoylglycerophosphoserine
2-palmitoylglycerophosphocholine
1-linoleoylglycerophosphoethanolamine
1-palmitoylglycerophosphoinositol
1-stearoylglycerophosphoinositol
Lysolipid
Caproate
Caprate
Medium Chain Fatty Acid
Deoxycarnitine
Carnitine
Carnitine Metabolism
chenodeoxycholate
Cholate
Primary Bile Acid Metabolism
3b-hydroxy-5-cholenoic acid
Hyocholate
Tauroursodeoxycholate
Ursodeoxycholate
12-dehydrocholate
3-dehydrocholate
Glycocholenate sulfate
Secondary Bile Acid Metabolism
Myristate
Arachidate
Stearate
Nervonate
Pentadecanoate
Oleate
Palmitoleate
Cis-vaccenate
Long Chain Fatty Acid
Fatty Acid Metabolism (Acyl Carnitine)
Decanoylcarnitine
Palmitoylcarnitine
3-carboxy-4-methyl-5-propyl-2-furanpropanoate
Hexadecanedioate
Undecanedioate
Fatty Acid, Dicarboxylate
Sterol
Lanosterol
Lathosterol
Inositol Metabolism
Myo-inositol
Fatty Acid, Monohydroxy
2-hydroxyoctanoate
9- & 13-HODE
2-hydroxypalmitate
Phospholipid Metabolism
Ethanolamine
Fatty Acid, Dihydroxy
9.10-DiHOME
Steroid
4-androsten-3alpha,17alpha-diol monosulfate
4-androsten-3beta,17beta-diol disulfate
5alpha-pregnan-3beta,20beta-diol monosulfate
Pregnenolone sulfate
4-androsten-3beta,17beta-diol monosulfate
5alpha-pregnan-3beta,20alpha-diol monosulfate
4-androsten-3beta,17beta-diol monosulfate
5alpha-pregnan-3(alpha or beta),20beta-diol disulfate

Figure S7. Significantly differentially enriched fecal metabolites amongst UC patients classified as MCS1, MCS2, MCS3, or MCS4 based on pairwise Welch's T-tests (p-value < 0.05).

Figure S8.

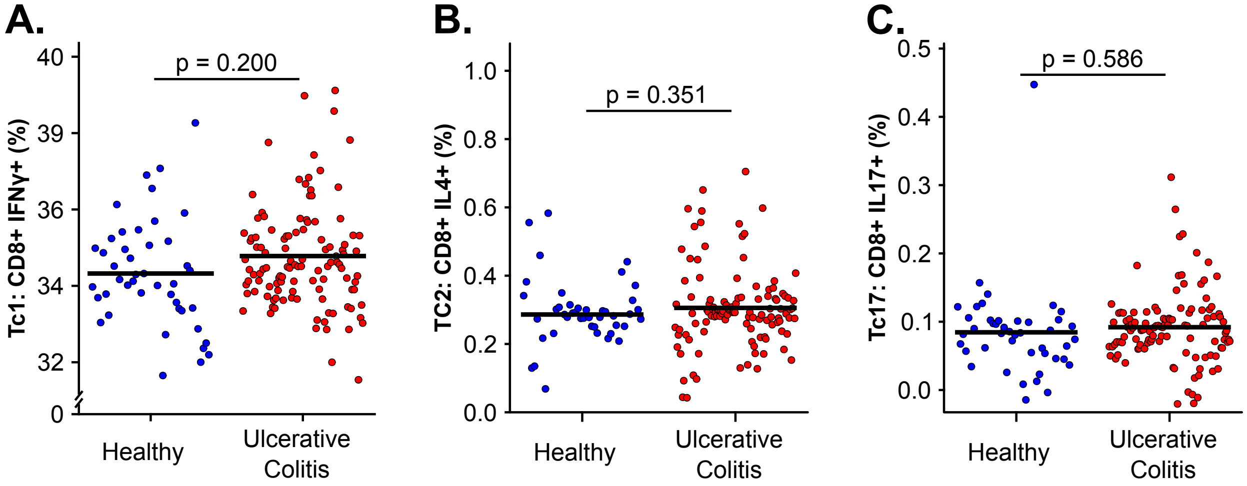

Figure S8. *In vitro* human T-cell activity following co-culture with autologous DCs challenged with sterilized fecal water. (A) Tc1 frequency, **(B)** Tc2 frequency, and **(C)** Tc17 frequency following challenge with Healthy (n = 48) or UC patient (n = 116) fecal water. Data generated from four replicate experiments using DC/T-cells obtained from four different, anonymous PBMC donors. Horizontal bars, representing mean fitted values for each group, and p-values were determined by linear mixed-effect modeling (see materials & methods).

Figure S9.

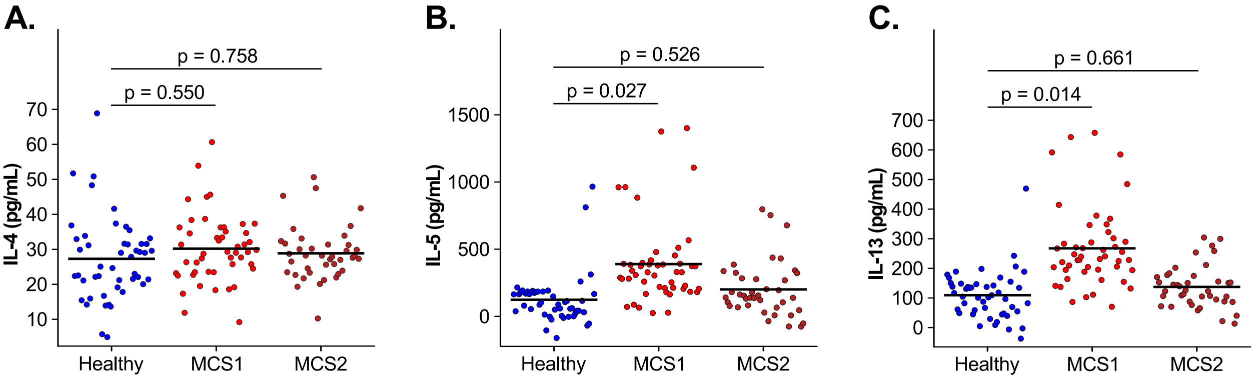

Figure S9. Concentrations of Th2 cytokines in cell supernatant following co-culture of human T-cells with autologous DCs challenged with sterilized fecal water. (A) IL-4, **(B)** IL-5, and **(C)** IL-13 (n = 48 for Healthy, 48 for MCS1, and 40 for MCS2). Data generated from two replicate experiments using DC/T-cells obtained from two anonymous PBMC donors. Horizontal bars (mean fitted values for each group) and P-values were determined by linear mixed-effect modeling (see materials & methods).

Table S1. Breakdown of Study Participant Cohort

	European (EU)	South Asian (SA)	Total
Healthy	10	3	13
Ulcerative Colitis	18	12	30

Table S2. Significantly differential Bacterial OTUs between UC patients and Healthy controls. Profiled by Illumina paired-end sequencing of the 16S rRNA gene. Table sorted by absolute change in abundance. Linear mixed-effects regression model p-value<0.05, q-value<0.3.

OTU	Phylum	Class	Order	Family	Genus	Change in Abundance (Control - Patient)	Selected Model	pvalue	qvalue
3943186	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unassigned	514.1872	NB	0.0000	0.0000
4397200	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	379.3179	ZINB	0.0000	0.0000
4326870	Firmicutes	Clostridia	Clostridiales	Veillonellaceae	Dialister	143.5128	ZINB	0.0000	0.0000
4368484	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unassigned	94.5487	NB	0.0003	0.0480
180825	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	55.7026	NB	0.0032	0.2895
187945	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unassigned	53.5897	NB	0.0000	0.0000
193969	Firmicutes	Clostridia	Clostridiales	unassigned	unassigned	49.7128	NB	0.0000	0.0000
299882	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	47.4282	ZINB	0.0000	0.0000
4323124	Bacteroidetes	Bacteroidia	Bacteroidales	[Barnesiellaceae]	unassigned	41.0641	NB	0.0001	0.0260
New.CleanUp.ReferenceOTU47735	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	40.3513	ZINB	0.0000	0.0000
354574	Proteobacteria	Deltaproteobacteria	Desulfovibrionales	Desulfovibrionaceae	Bilophila	39.9308	NB	0.0002	0.0416
1906635	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	39.8718	NB	0.0004	0.0588
183457	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unassigned	36.8205	NB	0.0000	0.0027
194597	Firmicutes	Clostridia	Clostridiales	unassigned	unassigned	35.5923	ZINB	0.0000	0.0000
312969	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	27.7872	ZINB	0.0007	0.0922
New.CleanUp.ReferenceOTU33034	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	26.1897	NB	0.0014	0.1602
148279	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Blautia	23.4846	NB	0.0005	0.0622
520657	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	22.8308	ZINB	0.0000	0.0000
4299126	Proteobacteria	Alphaproteobacteria	RF32	unassigned	unassigned	18.1974	NB	0.0031	0.2816
174912	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Coprococcus	16.0436	ZINB	0.0000	0.0004
271214	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	12.9667	ZINB	0.0000	0.0009
4341056	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unassigned	12.0436	ZINB	0.0000	0.0011

173744	Firmicutes	Clostridia	Clostridiales	Veillonellaceae	Megasphaera	11.8128	ZINB	0.0000	0.0012
195029	Firmicutes	Clostridia	Clostridiales	unassigned	unassigned	11.0872	NB	0.0004	0.0595
348612	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	10.8538	ZINB	0.0002	0.0412
189860	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Roseburia	10.0462	NB	0.0004	0.0614
New.Reference OTU256	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	9.7744	ZINB	0.0000	0.0000
276484	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	9.7026	NB	0.0000	0.0044
New.Reference OTU200	Bacteroidetes	Bacteroidia	Bacteroidales	unassigned	unassigned	9.4564	ZINB	0.0000	0.0001
318131	Firmicutes	Clostridia	Clostridiales	unassigned	unassigned	8.4564	NB	0.0032	0.2895
562244	Proteobacteria	Betaproteobacteria	Burkholderiales	Alcaligenaceae	Sutterella	8.0256	ZINB	0.0000	0.0000
4414725	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Blautia	7.2410	NB	0.0003	0.0438
4336943	Bacteroidetes	Bacteroidia	Bacteroidales	Rikenellaceae	unassigned	5.7897	ZINB	0.0000	0.0000
New.CleanUp. ReferenceOTU 4302	Bacteroidetes	Bacteroidia	Bacteroidales	S24-7	unassigned	4.8667	ZINB	0.0028	0.2672
249776	Firmicutes	Clostridia	Clostridiales	unassigned	unassigned	4.7667	ZINB	0.0017	0.1840
113542	Proteobacteria	Deltaproteobacteria	Desulfovibrionales	Desulfovibrionaceae	Desulfovibrio	4.7641	ZINB	0.0000	0.0000
4444262	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unassigned	4.5385	ZINB	0.0003	0.0456
New.CleanUp. ReferenceOTU 26055	Bacteroidetes	Bacteroidia	Bacteroidales	S24-7	unassigned	4.4718	ZINB	0.0002	0.0375
25842	Firmicutes	Clostridia	Clostridiales	unassigned	unassigned	4.3256	ZINB	0.0000	0.0001
4352242	Cyanobacteria	4C0d-2	YS2	unassigned	unassigned	3.9179	ZINB	0.0012	0.1398
4478840	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	unassigned	3.8667	ZINB	0.0028	0.2672
New.CleanUp. ReferenceOTU 22230	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unassigned	3.8128	ZINB	0.0002	0.0320
New.CleanUp. ReferenceOTU 63196	Bacteroidetes	Bacteroidia	Bacteroidales	[Barnesiellaceae]	unassigned	3.7462	ZINB	0.0000	0.0054
331150	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unassigned	3.5538	ZINB	0.0001	0.0122
New.CleanUp. ReferenceOTU 31094	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Roseburia	3.3615	NB	0.0031	0.2816
2046330	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unassigned	3.2744	NB	0.0009	0.1144
291090	Bacteroidetes	Bacteroidia	Bacteroidales	Porphyromonadaceae	Parabacteroides	3.2615	ZINB	0.0000	0.0003
583656	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	3.1513	ZINB	0.0002	0.0416
208972	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	3.0538	ZINB	0.0001	0.0172
New.CleanUp. ReferenceOTU 10421	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	3.0436	ZINB	0.0002	0.0375
617216	Actinobacteria	Coriobacteriia	Coriobacteriales	Coriobacteriaceae	unassigned	2.9872	ZINB	0.0000	0.0036
851668	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	2.6128	ZINB	0.0001	0.0264
186077	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Roseburia	2.5949	ZINB	0.0000	0.0077
215670	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	2.5051	ZINB	0.0003	0.0438
177153	Firmicutes	Clostridia	Clostridiales	unassigned	unassigned	2.2615	ZINB	0.0002	0.0352
350189	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unassigned	2.1974	NB	0.0008	0.1059
185864	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unassigned	2.1821	NB	0.0019	0.1991
196577	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unassigned	2.1641	NB	0.0000	0.0101
846798	Bacteroidetes	Bacteroidia	Bacteroidales	[Barnesiellaceae]	unassigned	2.1513	ZINB	0.0007	0.0869
New.CleanUp. ReferenceOTU	Tenericutes	Mollicutes	RF39	unassigned	unassigned	1.8103	ZINB	0.0025	0.2484

34816									
194471	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unassigned	1.7641	NB	0.0020	0.2065
New.CleanUp.ReferenceOTU59542	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	1.7026	ZINB	0.0000	0.0099
355197	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unassigned	1.6231	NB	0.0011	0.1277
183054	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unassigned	1.4282	NB	0.0016	0.1742
586525	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unassigned	1.3949	ZINB	0.0001	0.0226
691423	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unassigned	1.3513	ZINB	0.0030	0.2784
New.CleanUp.ReferenceOTU37129	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unassigned	1.2744	NB	0.0023	0.2311
300628	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unassigned	1.2744	ZINB	0.0028	0.2672
New.CleanUp.ReferenceOTU3658	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Lachnobacterium	1.2179	ZINB	0.0009	0.1104
3221787	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unassigned	1.2128	ZINB	0.0027	0.2628
New.CleanUp.ReferenceOTU7994	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Coprococcus	1.1974	ZINB	0.0034	0.2987
213762	Firmicutes	Clostridia	Clostridiales	Christensenellaceae	unassigned	1.0103	ZINB	0.0004	0.0602
1077373	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	0.9769	ZINB	0.0000	0.0080
955102	Actinobacteria	Actinobacteria	Actinomycetales	Actinomycetaceae	Actinomyces	0.9641	ZINB	0.0000	0.0014
17311	Firmicutes	Clostridia	Clostridiales	Christensenellaceae	unassigned	0.9333	ZINB	0.0022	0.2311
190577	Firmicutes	Clostridia	Clostridiales	unassigned	unassigned	0.9179	Poisson	0.0023	0.2311
179414	Firmicutes	Clostridia	Clostridiales	unassigned	unassigned	0.8333	ZINB	0.0011	0.1277
New.CleanUp.ReferenceOTU31276	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	0.8000	Poisson	0.0011	0.1286
181254	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unassigned	0.7795	Poisson	0.0009	0.1144
344154	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	0.6667	ZINB	0.0008	0.0958
New.CleanUp.ReferenceOTU35702	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Ruminococcus	0.6359	Poisson	0.0031	0.2804
New.ReferenceOTU275	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	0.2487	ZINB	0.0002	0.0419
195123	Bacteroidetes	Bacteroidia	Bacteroidales	Porphyromonadaceae	Parabacteroides	-0.0718	ZINB	0.0000	0.0004
1106290	Firmicutes	Clostridia	Clostridiales	unassigned	unassigned	-0.0949	ZINB	0.0002	0.0296
4420206	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Oscillospira	-0.2154	ZINB	0.0001	0.0263
New.CleanUp.ReferenceOTU16046	Firmicutes	Clostridia	Clostridiales	unassigned	unassigned	-0.2256	ZINB	0.0003	0.0438
New.CleanUp.ReferenceOTU2434	Firmicutes	Clostridia	Clostridiales	unassigned	unassigned	-0.3385	ZINB	0.0024	0.2441
360730	Bacteroidetes	Bacteroidia	Bacteroidales	[Odoribacteraceae]	Butyricimonas	-0.3590	ZINB	0.0000	0.0099
New.CleanUp.ReferenceOTU41650	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unassigned	-0.4564	ZINB	0.0001	0.0279
2820255	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unassigned	-0.5692	ZINB	0.0021	0.2143
230421	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unassigned	-0.6308	ZINB	0.0034	0.2987
New.CleanUp.ReferenceOTU30740	Firmicutes	Clostridia	Clostridiales	unassigned	unassigned	-0.6590	ZINB	0.0003	0.0419
174885	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unassigned	-0.7231	ZINB	0.0025	0.2452
New.ReferenceOTU55	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Coprococcus	-0.7256	ZINB	0.0034	0.2987
4343005	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Erwinia	-0.8231	ZINB	0.0017	0.1868

New.CleanUp.ReferenceOTU36094	Firmicutes	Clostridia	Clostridiales	Veillonellaceae	Megasphaera	-0.8231	ZINB	0.0017	0.1868
3856404	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Ruminococcus	-0.9256	ZINB	0.0000	0.0000
151623	Firmicutes	Clostridia	Clostridiales	Veillonellaceae	Megasphaera	-1.0436	ZINB	0.0000	0.0000
810831	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unassigned	-1.1231	ZINB	0.0007	0.0869
289958	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unassigned	-1.1667	ZINB	0.0000	0.0000
315223	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Anaerotruncus	-1.2692	ZINB	0.0000	0.0000
3121406	Synergistetes	Synergistia	Synergistales	Synergistaceae	unassigned	-1.3897	ZINB	0.0003	0.0489
732765	Bacteroidetes	Bacteroidia	Bacteroidales	Rikenellaceae	unassigned	-1.3897	ZINB	0.0003	0.0489
370086	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unassigned	-1.5590	ZINB	0.0000	0.0000
414949	Actinobacteria	Coriobacteriia	Coriobacteriales	Coriobacteriaceae	Collinsella	-1.7256	ZINB	0.0005	0.0665
158321	Firmicutes	Clostridia	Clostridiales	unassigned	unassigned	-1.9897	ZINB	0.0001	0.0211
580907	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unassigned	-2.0897	ZINB	0.0023	0.2311
130763	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unassigned	-2.2128	ZINB	0.0014	0.1600
95502	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Oscillospira	-2.3359	ZINB	0.0031	0.2804
295485	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unassigned	-2.3897	ZINB	0.0028	0.2672
New.CleanUp.ReferenceOTU10241	Firmicutes	Clostridia	Clostridiales	unassigned	unassigned	-2.6231	ZINB	0.0000	0.0084
New.CleanUp.ReferenceOTU45318	Firmicutes	Bacilli	Lactobacillales	Enterococcaceae	Enterococcus	-2.6795	ZINB	0.0000	0.0004
4376828	Actinobacteria	Actinobacteria	Bifidobacteriales	Bifidobacteriaceae	Bifidobacterium	-2.9026	NB	0.0023	0.2334
300829	Firmicutes	Clostridia	Clostridiales	Veillonellaceae	Dialister	-3.7897	ZINB	0.0000	0.0024
New.CleanUp.ReferenceOTU54255	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unassigned	-4.2385	ZINB	0.0000	0.0000
4319785	Bacteroidetes	Bacteroidia	Bacteroidales	[Paraprevotellaceae]	unassigned	-4.2821	ZINB	0.0000	0.0000
New.ReferenceOTU150	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	-4.3897	ZINB	0.0016	0.1742
4310223	Bacteroidetes	Bacteroidia	Bacteroidales	unassigned	unassigned	-4.6487	ZINB	0.0003	0.0480
4459940	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unassigned	-4.8026	ZINB	0.0002	0.0349
4473883	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	-5.2231	ZINB	0.0004	0.0514
4178726	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Blautia	-5.3564	ZINB	0.0000	0.0007
4305923	Tenericutes	Mollicutes	RF39	unassigned	unassigned	-5.4436	ZINB	0.0000	0.0000
New.ReferenceOTU380	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Lachnospira	-5.5077	NB	0.0005	0.0690
New.CleanUp.ReferenceOTU58906	Firmicutes	Clostridia	Clostridiales	Veillonellaceae	unassigned	-6.0615	ZINB	0.0000	0.0009
536866	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	-6.2436	NB	0.0001	0.0276
4413347	Actinobacteria	Actinobacteria	Bifidobacteriales	Bifidobacteriaceae	Bifidobacterium	-6.7615	NB	0.0003	0.0480
New.CleanUp.ReferenceOTU6065	Firmicutes	Clostridia	Clostridiales	unassigned	unassigned	-6.8692	ZINB	0.0000	0.0000
New.ReferenceOTU311	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	-6.8897	ZINB	0.0000	0.0003
157631	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unassigned	-6.9897	ZINB	0.0006	0.0734
304472	Firmicutes	Clostridia	Clostridiales	unassigned	unassigned	-7.0564	ZINB	0.0000	0.0002
270200	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	unassigned	-7.3026	NB	0.0025	0.2484
194995	Firmicutes	Clostridia	Clostridiales	unassigned	unassigned	-7.8231	NB	0.0029	0.2717
588471	Verrucomicrobia	Verrucomicrobiae	Verrucomicrobiales	Verrucomicrobiaceae	Akkermansia	-8.5231	ZINB	0.0000	0.0001

192070	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	-8.9436	ZINB	0.0003	0.0489
54794	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	-10.1718	NB	0.0000	0.0054
925131	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	-10.4410	ZINB	0.0000	0.0000
548503	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unassigned	-12.9385	ZINB	0.0000	0.0000
4420417	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unassigned	-15.9231	NB	0.0002	0.0416
606927	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	unassigned	-16.3051	NB	0.0003	0.0470
546557	Bacteroidetes	Bacteroidia	Bacteroidales	[Paraprevotellaceae]	[Prevotella]	-18.6205	ZINB	0.0000	0.0000
544419	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Lactococcus	-20.8564	NB	0.0010	0.1156
4458959	Firmicutes	Clostridia	Clostridiales	Veillonellaceae	Veillonella	-24.5256	NB	0.0018	0.1932
188348	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unassigned	-24.9462	ZINB	0.0000	0.0036
189828	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unassigned	-29.7897	ZINB	0.0026	0.2570
544996	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Oscillospira	-30.8538	NB	0.0009	0.1144
64384	Firmicutes	Bacilli	Lactobacillales	Leuconostocaceae	unassigned	-32.5564	NB	0.0020	0.2075
1010113	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unassigned	-35.8692	ZINB	0.0000	0.0004
170462	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	[Ruminococcus]	-38.4231	NB	0.0000	0.0009
188851	Bacteroidetes	Bacteroidia	Bacteroidales	S24-7	unassigned	-38.8000	ZINB	0.0000	0.0010
681370	Actinobacteria	Actinobacteria	Bifidobacteriales	Bifidobacteriaceae	Bifidobacterium	-39.6769	NB	0.0007	0.0882
4374302	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Dorea	-49.5744	ZINB	0.0002	0.0354
4300127	Firmicutes	Clostridia	Clostridiales	Veillonellaceae	Mitsuokella	-50.7487	ZINB	0.0000	0.0013
4424239	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	-51.6462	NB	0.0004	0.0614
4382476	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	-54.5897	ZINB	0.0000	0.0000
189092	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Faecalibacterium	-63.3667	ZINB	0.0010	0.1174
175844	Bacteroidetes	Bacteroidia	Bacteroidales	[Barnesiellaceae]	unassigned	-72.0462	ZINB	0.0000	0.0074
2943548	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Ruminococcus	-76.6692	ZINB	0.0000	0.0066
188676	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unassigned	-77.9846	ZINB	0.0003	0.0438
1033413	Firmicutes	Bacilli	Lactobacillales	Enterococcaceae	Enterococcus	-87.3846	NB	0.0033	0.2932
685156	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	-109.5359	NB	0.0003	0.0487
4300206	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	-166.0128	ZINB	0.0002	0.0416
1100972	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Lactococcus	-248.0462	NB	0.0000	0.0000
610111	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	-586.1923	NB	0.0000	0.0036
4425214	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	-629.0974	NB	0.0000	0.0112
72820	Actinobacteria	Actinobacteria	Bifidobacteriales	Bifidobacteriaceae	Bifidobacterium	-1743.6667	NB	0.0019	0.2006

Table S3. Significantly differential Bacterial OTUs between UC patients and Healthy controls profiled by PhyloChip microarray. Table sorted by fold change in abundance. T-test p-value<0.05, q-value<0.3.

OTU	Phylum	Class	Order	Family	Genus	Fold Change in Abundance (Patient / Control)	pvalue	qvalue
45477	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	4.7559	0.0027	0.2839
45235	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	4.1381	0.0012	0.2274
44435	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	3.9613	0.0014	0.2321
44466	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	3.9399	0.0023	0.2618
45425	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	3.3382	0.0021	0.2522
44576	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	3.2700	0.0012	0.2274
45713	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	3.0953	0.0029	0.2857
45205	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	2.9651	0.0028	0.2857
26934	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	2.9648	0.0011	0.2258
45709	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	2.9442	0.0012	0.2274
44335	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	2.8903	0.0011	0.2258
44900	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	2.8843	0.0019	0.2522
44906	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	2.7938	0.0033	0.2946
45489	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	2.7598	0.0015	0.2324
44503	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	2.7540	0.0007	0.2228
45143	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	2.7422	0.0003	0.1782
45026	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	2.7168	0.0004	0.1964
44540	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	2.6992	0.0010	0.2258
45746	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	2.6365	0.0009	0.2258
45572	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	2.5557	0.0012	0.2274
45659	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	2.5050	0.0006	0.2089
44659	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	2.4929	0.0006	0.2089
48408	Firmicutes	Bacilli	Bacillales	Bacillaceae	unclassified	2.4668	0.0032	0.2928
59382	Proteobacteria	Alphaproteobacteria	Rhizobiales	unclassified	sfA	2.4580	0.0020	0.2522
44370	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	2.4480	0.0020	0.2522
45552	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	2.4469	0.0007	0.2228
45617	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	2.3791	0.0017	0.2362
71848	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	2.3565	0.0023	0.2618
44197	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	2.3504	0.0030	0.2896
71961	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	2.3417	0.0020	0.2522
44689	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	2.2919	0.0009	0.2258

45134	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	2.2910	0.0025	0.2784
44331	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	2.2793	0.0010	0.2258
45607	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	2.2766	0.0007	0.2228
44343	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	2.2550	0.0014	0.2321
44609	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	2.2478	0.0029	0.2857
44421	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	2.2399	0.0009	0.2258
45398	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	2.2254	0.0027	0.2839
45865	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	2.1718	0.0006	0.2151
44167	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	2.1009	0.0019	0.2522
45824	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	2.0414	0.0012	0.2274
44535	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	2.0375	0.0014	0.2321
44971	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	2.0051	0.0017	0.2362
46394	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.9721	0.0008	0.2258
44841	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.9674	0.0024	0.2763
44226	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.9418	0.0019	0.2522
44964	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.9298	0.0014	0.2321
42991	Firmicutes	Bacilli	Lactobacillales	Enterococcaceae	Tetragenococcus	1.9152	0.0014	0.2321
19921	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	1.9056	0.0021	0.2532
45322	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.8877	0.0011	0.2268
44462	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.8868	0.0015	0.2321
45717	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.8674	0.0016	0.2324
45295	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.8580	0.0033	0.2955
45125	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.8525	0.0014	0.2321
45753	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.8478	3.49E-06	0.0333
45669	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.8325	0.0008	0.2258
45060	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.8277	0.0006	0.2151
45298	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.8017	0.0005	0.2049
45150	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.7853	0.0029	0.2857
44774	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.7664	0.0010	0.2258
45259	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.7529	0.0004	0.1900
72595	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	1.7434	0.0023	0.2618
39675	Actinobacteria	Actinobacteria	Actinomycetales	Streptomycetaceae	Streptomyces	1.7406	0.0033	0.2946
45649	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.7394	0.0025	0.2784
44648	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.7239	0.0008	0.2258
45340	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.7205	0.0025	0.2784
44248	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.7166	0.0027	0.2839
48311	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.7150	0.0031	0.2912
45351	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.7121	0.0014	0.2321
44722	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.7094	0.0021	0.2522
43083	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Lactococcus	1.7065	0.0005	0.2082

57814	Firmicutes	Clostridia	SHA-98	unclassified	sfA	1.6990	0.0001	0.1200
59279	Proteobacteria	Alphaproteobacteria	Rhodospirillales	Rhodospirillaceae	unclassified	1.6965	0.0004	0.1968
46236	Firmicutes	Bacilli	Bacillales	Paenibacillaceae	Ammoniphilus	1.6839	7.57E-06	0.0374
47111	Firmicutes	Bacilli	Bacillales	Staphylococcaceae	Staphylococcus	1.6804	0.0005	0.2049
45064	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.6750	0.0001	0.1178
44871	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.6628	0.0003	0.1782
44676	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.6590	0.0019	0.2522
45344	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.6402	0.0013	0.2274
45479	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.6384	0.0014	0.2321
71281	Firmicutes	Clostridia	Clostridiales	Clostridiales Family XI. Incertae Sedis	Anaerococcus	1.6369	0.0009	0.2258
48883	Firmicutes	Bacilli	Thermicanales	Thermicanaceae	unclassified	1.6282	0.0023	0.2652
45892	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.6190	0.0008	0.2258
44460	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.6073	4.17E-05	0.0917
72204	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	1.6032	0.0025	0.2778
59041	Proteobacteria	Alphaproteobacteria	Rhodospirillales	Rhodospirillaceae	Rhodospirillum	1.6005	0.0030	0.2896
72807	Firmicutes	Bacilli	Lactobacillales	Leuconostocaceae	Leuconostoc	1.5944	0.0012	0.2274
44643	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.5865	0.0002	0.1591
44168	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.5811	0.0026	0.2822
70882	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	Clostridium	1.5787	0.0015	0.2321
45673	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.5544	0.0021	0.2522
44580	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.5530	0.0011	0.2258
44387	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.5475	0.0017	0.2362
44644	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.5452	0.0030	0.2896
26692	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	1.5451	0.0016	0.2324
45491	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.5441	0.0002	0.1728
45032	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.5428	0.0001	0.1203
40870	Actinobacteria	Actinobacteria	Actinomycetales	ACK-M1	unclassified	1.5319	0.0020	0.2522
43663	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Lactococcus	1.5311	0.0002	0.1476
47433	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.5264	0.0029	0.2857
42521	Firmicutes	Bacilli	Lactobacillales	Enterococcaceae	Enterococcus	1.5257	0.0008	0.2258
45513	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.5240	2.17E-05	0.0612
46141	Firmicutes	Bacilli	Bacillales	Staphylococcaceae	Staphylococcus	1.5233	0.0003	0.1782
44344	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.5217	0.0012	0.2274
44162	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.5135	0.0021	0.2522
45336	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.5058	0.0004	0.1964
36880	Actinobacteria	Actinobacteria	Actinomycetales	Corynebacteriaceae	Corynebacterium	1.5001	0.0016	0.2324
37116	Actinobacteria	Actinobacteria	Actinomycetales	Corynebacteriaceae	Corynebacterium	1.4997	0.0028	0.2853
72785	Firmicutes	Bacilli	Lactobacillales	Carnobacteriaceae	Trichococcus	1.4995	0.0031	0.2928
47246	Firmicutes	Bacilli	Bacillales	Staphylococcaceae	Staphylococcus	1.4967	0.0025	0.2775
72006	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	1.4961	0.0007	0.2228

45503	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.4949	0.0020	0.2522
49560	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.4935	0.0027	0.2839
44209	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.4878	0.0012	0.2274
47560	Firmicutes	Bacilli	Bacillales	Staphylococcaceae	Staphylococcus	1.4825	0.0026	0.2791
45469	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.4758	0.0025	0.2784
45248	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.4724	0.0027	0.2839
45391	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.4720	0.0003	0.1782
45004	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.4683	0.0021	0.2522
30437	Actinobacteria	Actinobacteria	Actinomycetales	Corynebacteriaceae	Corynebacterium	1.4675	0.0014	0.2321
72227	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	1.4639	0.0029	0.2872
45255	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.4582	0.0014	0.2321
45872	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.4569	0.0001	0.1476
45577	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.4567	0.0001	0.1476
44279	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.4547	0.0011	0.2258
69306	Firmicutes	Clostridia	Clostridiales	Clostridiales Family XI. Incertae Sedis	Tissierella	1.4494	0.0011	0.2258
45886	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.4490	0.0010	0.2258
45414	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.4444	0.0011	0.2258
45647	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.4436	0.0011	0.2258
45524	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.4400	0.0016	0.2324
44834	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.4378	0.0014	0.2321
44986	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.4372	0.0005	0.2082
49780	Firmicutes	Bacilli	Bacillales	Bacillaceae	unclassified	1.4187	0.0006	0.2089
70740	Firmicutes	Clostridia	Clostridiales	Clostridiales Family XI. Incertae Sedis	Anaerococcus	1.4155	0.0005	0.2089
47350	Firmicutes	Bacilli	Bacillales	Bacillaceae	Geobacillus	1.4119	0.0030	0.2896
43316	Firmicutes	Bacilli	Lactobacillales	Enterococcaceae	Enterococcus	1.4109	0.0003	0.1835
36942	Actinobacteria	Actinobacteria	Actinomycetales	Corynebacteriaceae	Corynebacterium	1.4107	0.0013	0.2321
43264	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.4096	4.97E-05	0.0983
45854	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.4032	0.0027	0.2839
45241	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.3979	0.0004	0.1968
71260	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	Clostridium	1.3939	0.0006	0.2089
45123	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.3936	0.0001	0.1476
42906	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.3925	3.65E-09	0.0001
44321	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.3913	0.0010	0.2258
37217	Actinobacteria	Actinobacteria	Actinomycetales	Corynebacteriaceae	Corynebacterium	1.3873	0.0011	0.2258
44862	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.3852	0.0010	0.2258
44927	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.3836	0.0002	0.1591
70053	Firmicutes	Clostridia	Clostridiales	Clostridiales Family XII. Incertae Sedis	unclassified	1.3833	0.0016	0.2324
27556	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Ruminococcus	1.3807	0.0026	0.2784
44772	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.3789	0.0019	0.2522
58619	Gemmatimonadetes	Gemmatimonadetes	Gemmatimonadales	Gemmatimonadaceae	unclassified	1.3749	0.0002	0.1591

45014	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.3735	0.0017	0.2362
45778	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.3713	0.0030	0.2896
45254	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.3673	0.0007	0.2228
72718	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	Clostridium	1.3666	0.0002	0.1728
42913	Firmicutes	Bacilli	Lactobacillales	Enterococcaceae	Vagococcus	1.3585	0.0010	0.2258
44281	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.3530	1.42E-05	0.0468
49897	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.3517	0.0014	0.2321
45157	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.3512	5.06E-06	0.0333
44480	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.3485	0.0007	0.2228
70161	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	1.3419	0.0033	0.2946
44400	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.3415	0.0025	0.2775
72147	Firmicutes	Bacilli	Lactobacillales	Leuconostocaceae	Leuconostoc	1.3403	0.0027	0.2839
46309	Firmicutes	Bacilli	Bacillales	Staphylococcaceae	Staphylococcus	1.3332	0.0029	0.2872
44551	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.3209	3.03E-05	0.0749
71475	Tenericutes	Erysipelotrichi	Erysipelotrichales	Erysipelotrichaceae	Clostridium	1.3198	0.0018	0.2518
45792	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.3195	0.0029	0.2857
45137	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.3161	9.97E-06	0.0394
72154	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	1.3127	0.0023	0.2656
72265	Firmicutes	Bacilli	Lactobacillales	Leuconostocaceae	Leuconostoc	1.3017	0.0006	0.2089
45590	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.3006	0.0033	0.2946
51660	Acidobacteria	Acidobacteria	Acidobacteriales	Acidobacteriaceae	unclassified	1.2863	0.0003	0.1782
35240	Actinobacteria	Actinobacteria	Actinomycetales	Corynebacteriaceae	Corynebacterium	1.2854	0.0001	0.1476
37623	Actinobacteria	Actinobacteria	Actinomycetales	Gordoniaceae	Gordonia	1.2825	0.0003	0.1728
45542	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.2791	0.0008	0.2258
22253	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Clostridium	1.2790	0.0020	0.2522
45760	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.2763	0.0020	0.2522
72208	Firmicutes	Bacilli	Lactobacillales	Carnobacteriaceae	Trichococcus	1.2749	0.0001	0.1200
69273	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	1.2704	0.0002	0.1591
40803	Actinobacteria	Actinobacteria	Actinomycetales	Micrococcaceae	Citricoccus	1.2668	0.0015	0.2324
70908	Firmicutes	Clostridia	Clostridiales	Clostridiales Family XI. Incertae Sedis	Anaerococcus	1.2662	0.0015	0.2321
49198	Firmicutes	Bacilli	Bacillales	unclassified	sfE	1.2592	0.0009	0.2258
19135	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Clostridium	1.2551	0.0020	0.2522
44868	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	1.2521	0.0004	0.1964
48368	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.2435	0.0001	0.1476
74076	Tenericutes	Mollicutes	Acholeplasmatales	Acholeplasmataceae	Candidatus Phytoplasma	1.2426	0.0021	0.2522
43878	Firmicutes	Bacilli	Bacillales	Bacillaceae	Bacillus	1.2406	0.0010	0.2258
44144	Actinobacteria	Actinobacteria	Acidimicrobiales	Acidimicrobiaceae	unclassified	1.2366	0.0011	0.2258
28185	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	1.2286	0.0008	0.2258
28322	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	1.2273	0.0016	0.2362
53960	Chloroflexi	Anaerolineae	Anaerolineales	Anaerolinaceae	A4b	1.2137	0.0020	0.2522

17659	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Roseburia	1.2132	0.0032	0.2946
23121	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Butyrivibrio	0.8323	0.0033	0.2946
19712	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Coprococcus	0.7854	0.0021	0.2544
21058	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Blautia	0.7562	0.0013	0.2283
68181	Bacteroidetes	Bacteroidia	Bacteroidales	RikenellaceaeII	unclassified	0.7408	0.0020	0.2522
18864	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Clostridium	0.7361	0.0033	0.2946
18999	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Ruminococcus	0.7319	0.0011	0.2258
66718	Bacteroidetes	Sphingobacteria	Sphingobacteriales	Flexibacteraceae	unclassified	0.7237	0.0003	0.1728
18809	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.7213	0.0028	0.2853
15307	Proteobacteria	Betaproteobacteria	Burkholderiales	Oxalobacteraceae	Oxalobacter	0.6976	0.0016	0.2324
21514	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Blautia	0.6564	0.0031	0.2912
14835	Proteobacteria	Betaproteobacteria	Neisseriales	Neisseriaceae	unclassified	0.6425	0.0008	0.2258
15138	Proteobacteria	Betaproteobacteria	Burkholderiales	Oxalobacteraceae	Oxalobacter	0.6311	0.0015	0.2324
66495	Bacteroidetes	Flavobacteria	Flavobacteriales	Flavobacteriaceae	Muricauda	0.6304	0.0033	0.2946
69456	Bacteroidetes	Bacteroidia	Bacteroidales	Rikenellaceae	Alistipes	0.6267	0.0033	0.2946
51056	Acidobacteria	Acidobacteria	Acidobacteriales	Acidobacteriaceae	unclassified	0.6260	0.0009	0.2258
75329	Bacteroidetes	Sphingobacteria	Sphingobacteriales	Chitinophagaceae	unclassified	0.6210	0.0031	0.2901
72073	Proteobacteria	Alphaproteobacteria	Rickettsiales	Rickettsiaceae	Wolbachia	0.6192	0.0022	0.2618
69796	Bacteroidetes	Bacteroidia	Bacteroidales	Porphyromonadaceae	Parabacteroides	0.6123	0.0012	0.2274
18696	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Ruminococcus	0.6000	0.0009	0.2258
69312	Bacteroidetes	Bacteroidia	Bacteroidales	Rikenellaceae	Alistipes	0.5763	0.0005	0.2089
68544	Bacteroidetes	Bacteroidia	Bacteroidales	Rikenellaceae	unclassified	0.5631	0.0003	0.1728
19189	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Ruminococcus	0.5573	0.0018	0.2470
69349	Bacteroidetes	Bacteroidia	Bacteroidales	Rikenellaceae	Alistipes	0.5282	0.0017	0.2435
69646	Bacteroidetes	Bacteroidia	Bacteroidales	Porphyromonadaceae	Parabacteroides	0.5256	0.0004	0.1964
69838	Bacteroidetes	Bacteroidia	Bacteroidales	Porphyromonadaceae	Parabacteroides	0.5125	0.0010	0.2258
68579	Bacteroidetes	Bacteroidia	Bacteroidales	Rikenellaceae	unclassified	0.4983	0.0030	0.2896
68463	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	0.4915	0.0003	0.1782
19221	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Ruminococcus	0.4793	0.0009	0.2258
19689	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	0.4544	0.0002	0.1476
5457	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Pantoea	0.3227	0.0028	0.2853
69144	Bacteroidetes	Bacteroidia	Bacteroidales	Porphyromonadaceae	Odoribacter	0.3035	0.0017	0.2362

Table S4. Significantly differential Fungal OTUs between UC patients and Healthy controls. Profiled by Illumina paired-end sequencing of the 16S rRNA gene. Table sorted by absolute change in abundance. Linear mixed-effects regression model p-value<0.05, q-value<0.3.

OTU	Phylum	Class	Order	Family	Genus	Change in Abundance (Control - Patient)	Selected Model	pvalue	qvalue
OTU_9	Ascomycota	Dothideomycetes	Pleosporales	Pleosporaceae	Alternaria	445.8487	NB	0.0010	0.0139
OTU_48	Ascomycota	Eurotiomycetes	Eurotiales	Trichocomaceae	Aspergillus	68.6308	ZINB	0.0079	0.0832
OTU_63	Ascomycota	Saccharomycetes	Saccharomycetales	Incertae sedis	Candida	56.0308	ZINB	0.0000	0.0000
OTU_123	Ascomycota	Eurotiomycetes	Eurotiales	Trichocomaceae	Aspergillus	44.7051	NB	0.0283	0.2763
OTU_84	Basidiomycota	Tremellomycetes	Trichosporonales	Trichosporonaceae	Trichosporon	32.8333	ZINB	0.0000	0.0000
OTU_39	Ascomycota	Eurotiomycetes	Eurotiales	Trichocomaceae	Talaromyces	12.9667	ZINB	0.0000	0.0003
OTU_87	Basidiomycota	Microbotryomycetes	Sporidiobolales	unassigned	unassigned	9.1872	ZINB	0.0024	0.0304
OTU_137	Ascomycota	Sordariomycetes	Glomerellales	Glomerellaceae	Glomerella	0.3026	ZINB	0.0000	0.0004
OTU_177	Ascomycota	Eurotiomycetes	Eurotiales	Trichocomaceae	Penicillium	-0.3590	ZINB	0.0037	0.0426
OTU_161	Basidiomycota	Tremellomycetes	Tremellales	Incertae sedis	Cryptococcus	-0.5487	ZINB	0.0004	0.0077
OTU_40	Basidiomycota	Agaricomycetes	Agaricales	Agaricaceae	Agaricus	-15.1821	ZINB	0.0001	0.0028
OTU_16	Ascomycota	Saccharomycetes	Saccharomycetales	Incertae sedis	Debaryomyces	-121.2154	ZINB	0.0005	0.0086
OTU_4	Ascomycota	Saccharomycetes	Saccharomycetales	Incertae sedis	Candida	-450.5128	ZINB	0.0000	0.0003

Table S5. Significantly differential Bacterial OTUs between UC-MCS. Profiled by Illumina paired-end sequencing of the ITS2 region. Table sorted by Kruskal-Wallis p-value (p-value<0.05, q-value<0.08). Linear mixed-effects regression models were applied to determine pairwise differences amongst UC-MCS **(**p-value<0.05).

OTU	Phylum	Class	Order	Family	Genus	MCS1-2 Model	MCS1-2 pvalue	MCS1-2 change	MCS1-3 Model	MCS1-3 pvalue	MCS1-3 change	MCS1-4 Model	MCS1-4 pvalue	MCS1-4 change
1147868	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9991	-1.33
161423	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	NB	0.0000	251.63	NB	0.0000	317.83	NB	0.0000	322.83
2942332	Firmicutes	Clostridia	Clostridiales	unclassified	unclassified	#N/A	NA	NA	Poisson	0.9986	-0.75	NA	NA	NA

New.CleanUp.ReferenceOTU4884	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	#N/A	NA	NA	Poisson	0.9977	-1.00	NA	NA	NA
New.CleanUp.ReferenceOTU32801	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	#N/A	NA	NA	ZINB	0.9901	-34.25	NA	NA	NA
176062	Firmicutes	Clostridia	Clostridiales	unclassified	unclassified	#N/A	NA	NA	ZINB	0.9902	-46.00	NA	NA	NA
New.CleanUp.ReferenceOTU50385	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	NB	0.0638	1.43	Poisson	0.9966	2.33	Poisson	0.9970	2.33
New.ReferenceOTU97	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	NB	0.0000	8.90	NB	0.0002	9.75	NB	0.9968	12.00
301253	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	#N/A	NA	NA	ZINB	0.9938	-18.75	ZINB	0.9937	-20.67
4384058	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	ZINB	0.9937	-20.67
269125	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	NB	0.9975	-5.00
102049	Actinobacteria	Actinobacteria	Bifidobacteriales	Bifidobacteriaceae	Bifidobacterium	#N/A	NA	NA	NA	NA	NA	Poisson	0.9976	-2.00
New.CleanUp.ReferenceOTU375	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Lactococcus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-1.33
751643	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-1.00
New.CleanUp.ReferenceOTU24463	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-1.00
184464	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	#N/A	NA	NA	ZINB	0.9844	-98.50	ZINB	0.9971	-6.00
336372	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	#N/A	NA	NA	ZINB	0.9940	-28.00	ZINB	0.9982	-2.00
181539	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	#N/A	NA	NA	ZINB	0.9941	-26.50	Poisson	0.9977	-0.67
292041	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	#N/A	NA	NA	ZINB	0.9906	-26.25	Poisson	0.9964	-1.00
172777	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	NB	0.0342	17.97	NB	0.9976	27.67	NB	0.9967	27.67
173565	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	#N/A	NA	NA	Poisson	0.9977	-1.00	Poisson	0.9986	-0.33
2037235	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	#N/A	NA	NA	ZINB	0.9942	-18.00	ZINB	0.9971	-4.67
849535	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	ZINB	0.9071	-608.00	ZINB	0.9343	-1115.00	NA	NA	NA
211706	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	NB	0.0050	9.02	NB	0.9976	13.92	NB	0.0008	13.25
678717	Firmicutes	Clostridia	Clostridiales	unclassified	unclassified	Poisson	0.9981	0.08	Poisson	0.0004	-3.17	Poisson	0.9975	0.08
292057	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	NB	0.9975	-6.80	Poisson	0.9979	-0.25	NB	0.9982	-90.67
4389066	Firmicutes	Clostridia	Clostridiales	unclassified	unclassified	Poisson	0.9980	-0.10	Poisson	0.9976	-1.75	NA	NA	NA
297856	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	Poisson	0.9980	-0.10	Poisson	0.9962	-2.50	NA	NA	NA
New.ReferenceOTU320	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	Poisson	0.0019	1.70	Poisson	0.9966	2.00	Poisson	0.9954	2.00
New.ReferenceOTU69	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	NB	0.0117	3.47	NB	0.9978	4.17	NB	0.9970	4.17
4436552	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	Poisson	0.7965	-0.07	NB	0.0000	-1324.42	NB	0.0000	-3406.67
1992	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	ZINB	0.0000	70.55	ZINB	0.0027	55.75	ZINB	0.0014	75.75
1508541	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	NB	0.0061	15.87	NB	0.0000	22.17	NB	0.0002	22.83
326482	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	ZINB	0.9945	-5.40	ZINB	0.9845	-85.25	NA	NA	NA
3887769	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	NB	0.0061	2.75	Poisson	0.9945	4.25	Poisson	0.0117	3.92
184209	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	NB	0.0367	5.28	NB	0.0004	8.33	NB	0.9968	9.08
4289859	Firmicutes	Clostridia	Clostridiales	unclassified	unclassified	Poisson	0.9981	0.08	Poisson	0.0134	-1.17	Poisson	0.9975	0.08
304047	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	Poisson	0.9946	2.08	ZINB	0.9968	2.08	ZINB	0.9972	2.08

177222	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	NB	0.0012	24.70	NB	0.0001	29.00	NB	0.9967	29.50
New.ReferenceOTU308	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	NB	0.2080	2.60	NB	0.9964	6.50	NB	0.9969	6.50
192684	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	NB	0.0002	11.20	NB	0.9977	12.00	NB	0.9968	12.00
4318208	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	Poisson	0.9980	-0.10	ZINB	0.9737	-414.75	ZINB	0.9952	-15.67
157327	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	NB	0.0027	21.18	ZINB	0.0000	27.08	ZINB	0.0000	27.58
4381553	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	NB	0.6579	494.38	NB	0.0000	1570.83	NB	0.0000	1578.58
3426658	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	NB	0.0093	7.63	ZINB	0.0006	10.58	ZINB	0.9926	10.83
177134	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	ZINB	0.9967	-1.80	Poisson	0.9986	-0.75	NA	NA	NA
189588	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Blautia	NB	0.0128	-25.60	NB	0.0004	11.75	NB	0.0014	11.83
195028	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Blautia	NB	0.0008	-5.45	ZINB	0.9982	0.25	ZINB	0.9975	0.25
4295618	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	#N/A	NA	NA	Poisson	0.9977	-1.00	NA	NA	NA
New.CleanUp.ReferenceOTU35616	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	#N/A	NA	NA	Poisson	0.9977	-1.00	NA	NA	NA
New.CleanUp.ReferenceOTU58350	Firmicutes	Clostridia	Clostridiales	unclassified	unclassified	#N/A	NA	NA	Poisson	0.9977	-1.00	NA	NA	NA
4307391	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	#N/A	NA	NA	Poisson	0.9978	-0.50	NA	NA	NA
322803	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	#N/A	NA	NA	Poisson	0.9978	-0.50	NA	NA	NA
New.CleanUp.ReferenceOTU12268	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	unclassified	#N/A	NA	NA	Poisson	0.9978	-0.50	NA	NA	NA
New.CleanUp.ReferenceOTU16322	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	#N/A	NA	NA	Poisson	0.9978	-0.50	NA	NA	NA
New.CleanUp.ReferenceOTU22670	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	#N/A	NA	NA	Poisson	0.9978	-0.50	NA	NA	NA
New.CleanUp.ReferenceOTU22691	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Blautia	#N/A	NA	NA	Poisson	0.9978	-0.50	NA	NA	NA
New.CleanUp.ReferenceOTU24420	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	#N/A	NA	NA	Poisson	0.9978	-0.50	NA	NA	NA
New.CleanUp.ReferenceOTU33198	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	#N/A	NA	NA	Poisson	0.9978	-0.50	NA	NA	NA
New.CleanUp.ReferenceOTU37179	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Roseburia	#N/A	NA	NA	Poisson	0.9978	-0.50	NA	NA	NA
New.CleanUp.ReferenceOTU40515	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	#N/A	NA	NA	Poisson	0.9978	-0.50	NA	NA	NA
New.CleanUp.ReferenceOTU44096	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Lachnospira	#N/A	NA	NA	Poisson	0.9978	-0.50	NA	NA	NA
New.CleanUp.ReferenceOTU45187	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	#N/A	NA	NA	Poisson	0.9978	-0.50	NA	NA	NA
New.CleanUp.ReferenceOTU49976	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	#N/A	NA	NA	Poisson	0.9978	-0.50	NA	NA	NA
New.CleanUp.ReferenceOTU51098	Firmicutes	Erysipelotrichi	Erysipelotrichales	Erysipelotrichaceae	Catenibacterium	#N/A	NA	NA	Poisson	0.9978	-0.50	NA	NA	NA
New.CleanUp.ReferenceOTU52517	Firmicutes	Clostridia	Clostridiales	unclassified	unclassified	#N/A	NA	NA	Poisson	0.9978	-0.50	NA	NA	NA

New.CleanUp.ReferenceOTU53775	Firmicutes	Clostridia	Clostridiales	unclassified	unclassified	#N/A	NA	NA	Poisson	0.9978	-0.50	NA	NA	NA
New.CleanUp.ReferenceOTU60000	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	Clostridium	#N/A	NA	NA	Poisson	0.9978	-0.50	NA	NA	NA
New.CleanUp.ReferenceOTU60942	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	#N/A	NA	NA	Poisson	0.9978	-0.50	NA	NA	NA
193314	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Ruminococcus	#N/A	NA	NA	ZINB	0.9740	-121.00	NA	NA	NA
188851	Bacteroidetes	Bacteroidia	Bacteroidales	S24-7	unclassified	#N/A	NA	NA	ZINB	0.9764	-306.00	NA	NA	NA
4429981	Firmicutes	Clostridia	Clostridiales	unclassified	unclassified	#N/A	NA	NA	ZINB	0.9770	-172.00	NA	NA	NA
2403301	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	#N/A	NA	NA	ZINB	0.9857	-70.00	NA	NA	NA
337161	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	#N/A	NA	NA	ZINB	0.9860	-65.25	NA	NA	NA
New.CleanUp.ReferenceOTU23159	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	#N/A	NA	NA	ZINB	0.9903	-17.50	NA	NA	NA
584107	Firmicutes	Clostridia	Clostridiales	unclassified	unclassified	#N/A	NA	NA	ZINB	0.9948	-7.50	NA	NA	NA
771181	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	#N/A	NA	NA	ZINB	0.9948	-8.50	NA	NA	NA
849393	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	#N/A	NA	NA	ZINB	0.9957	-49.50	NA	NA	NA
176785	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Oscillospira	#N/A	NA	NA	Poisson	0.9963	-1.75	NA	NA	NA
New.CleanUp.ReferenceOTU22927	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	#N/A	NA	NA	Poisson	0.9963	-1.75	NA	NA	NA
New.CleanUp.ReferenceOTU23760	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	#N/A	NA	NA	Poisson	0.9963	-1.75	NA	NA	NA
New.CleanUp.ReferenceOTU44943	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	#N/A	NA	NA	Poisson	0.9963	-1.75	NA	NA	NA
New.CleanUp.ReferenceOTU49048	Bacteroidetes	Bacteroidia	Bacteroidales	[Paraprevotellaceae]	[Prevotella]	#N/A	NA	NA	ZINB	0.9963	-4.75	NA	NA	NA
303963	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	SMB53	#N/A	NA	NA	Poisson	0.9963	-1.50	NA	NA	NA
524444	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Blautia	#N/A	NA	NA	Poisson	0.9963	-1.50	NA	NA	NA
New.CleanUp.ReferenceOTU33015	Firmicutes	Clostridia	Clostridiales	unclassified	unclassified	#N/A	NA	NA	Poisson	0.9963	-1.50	NA	NA	NA
New.CleanUp.ReferenceOTU50199	Firmicutes	Clostridia	Clostridiales	unclassified	unclassified	#N/A	NA	NA	Poisson	0.9963	-1.25	NA	NA	NA
New.CleanUp.ReferenceOTU28012	Firmicutes	Clostridia	Clostridiales	unclassified	unclassified	#N/A	NA	NA	Poisson	0.9963	-1.25	NA	NA	NA
New.CleanUp.ReferenceOTU53899	Firmicutes	Erysipelotrichi	Erysipelotrichales	Erysipelotrichaceae	Catenibacterium	#N/A	NA	NA	Poisson	0.9964	-1.00	NA	NA	NA
336325	Firmicutes	Clostridia	Clostridiales	unclassified	unclassified	#N/A	NA	NA	Poisson	0.9964	-1.00	NA	NA	NA
1904497	Firmicutes	Clostridia	Clostridiales	unclassified	unclassified	#N/A	NA	NA	Poisson	0.9964	-1.00	NA	NA	NA
New.CleanUp.ReferenceOTU12247	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Ruminococcus	#N/A	NA	NA	Poisson	0.9964	-1.00	NA	NA	NA
New.CleanUp.ReferenceOTU21275	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	#N/A	NA	NA	Poisson	0.9964	-1.00	NA	NA	NA
New.CleanUp.ReferenceOTU40148	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	#N/A	NA	NA	Poisson	0.9964	-1.00	NA	NA	NA

New.CleanUp.ReferenceOTU64354	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	#N/A	NA	NA	Poisson	0.9964	-1.00	NA	NA	NA
4412542	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	#N/A	NA	NA	ZINB	0.9964	-2.25	NA	NA	NA
350627	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	#N/A	NA	NA	ZINB	0.9967	-4.25	NA	NA	NA
New.CleanUp.ReferenceOTU26300	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	#N/A	NA	NA	ZINB	0.9968	-5.75	NA	NA	NA
527941	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	#N/A	NA	NA	ZINB	0.9968	-5.00	NA	NA	NA
298451	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	#N/A	NA	NA	ZINB	0.9968	-5.00	NA	NA	NA
New.CleanUp.ReferenceOTU24195	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	#N/A	NA	NA	ZINB	0.9969	-3.50	NA	NA	NA
178640	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	SMB53	#N/A	NA	NA	ZINB	0.9969	-3.25	NA	NA	NA
591118	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	#N/A	NA	NA	NB	0.9976	-1.75	NA	NA	NA
New.CleanUp.ReferenceOTU38822	Firmicutes	Clostridia	Clostridiales	unclassified	unclassified	#N/A	NA	NA	NB	0.9976	-1.75	NA	NA	NA
New.CleanUp.ReferenceOTU43727	Firmicutes	Clostridia	Clostridiales	unclassified	unclassified	#N/A	NA	NA	Poisson	0.9977	-0.75	NA	NA	NA
New.CleanUp.ReferenceOTU42913	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	#N/A	NA	NA	Poisson	0.9977	-0.75	NA	NA	NA
New.CleanUp.ReferenceOTU59565	Bacteroidetes	Bacteroidia	Bacteroidales	S24-7	unclassified	#N/A	NA	NA	Poisson	0.9977	-0.75	NA	NA	NA
4446320	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	unclassified	#N/A	NA	NA	Poisson	0.9977	-0.75	NA	NA	NA
New.CleanUp.ReferenceOTU15349	Firmicutes	Clostridia	Clostridiales	unclassified	unclassified	#N/A	NA	NA	Poisson	0.9977	-0.75	NA	NA	NA
1768385	Firmicutes	Clostridia	Clostridiales	Peptostreptococcaceae	unclassified	#N/A	NA	NA	ZINB	0.9980	-2.25	NA	NA	NA
2920309	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	NB	0.0000	14.10	NB	0.0011	14.00	NB	0.9968	15.00
12574	Actinobacteria	Actinobacteria	Actinomycetales	Actinomycetaceae	Actinomyces	NB	0.0009	-11.83	NB	0.2963	1.92	NB	0.0000	-32.17
92535	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	Poisson	0.9980	-0.10	NA	NA	NA	Poisson	0.9962	-2.67
4404220	Proteobacteria	Gammaproteobacteria	Pasteurellales	Pasteurellaceae	Actinobacillus	Poisson	0.9980	-0.10	NA	NA	NA	Poisson	0.9977	-1.33
New.CleanUp.ReferenceOTU16318	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	Poisson	0.9980	-0.10	NA	NA	NA	ZINB	0.9943	-14.00
288680	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Lactococcus	Poisson	0.9980	-0.10	NA	NA	NA	Poisson	0.9962	-2.67
New.CleanUp.ReferenceOTU63593	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	Poisson	0.9949	0.92	Poisson	0.9949	0.92	Poisson	0.9956	0.92
553150	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Coprococcus	NB	0.0995	-5.42	ZINB	0.9952	1.08	ZINB	0.9958	1.08
4410166	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	Poisson	0.8943	-0.05	NB	0.0000	-12333.75	NB	0.0000	-593.92
15202	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	Poisson	0.9980	-0.10	NA	NA	NA	Poisson	0.9977	-1.33
297414	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	Poisson	0.9981	0.08	Poisson	0.0262	-0.92	ZINB	0.0000	-130.25
New.CleanUp.ReferenceOTU23917	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	ZINB	0.9878	-12.00	NB	0.9975	-6.00	NA	NA	NA
3600504	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	NB	0.0260	6159.57	ZINB	0.0001	7995.92	ZINB	0.0572	7978.17
327218	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	ZINB	0.9917	-7.00	NB	0.9975	-5.75	NA	NA	NA
182588	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Ruminococcus	ZINB	0.9950	-5.10	NB	0.9975	-8.25	NA	NA	NA

1121530	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	Poisson	0.9980	-0.10	NA	NA	NA	Poisson	0.9986	-0.67
567427	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	ZINB	0.9988	-0.30	NA	NA	NA	ZINB	0.9963	-4.33
180462	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Blautia	NB	0.1572	9.38	NB	0.0000	21.33	NB	0.0001	21.92
724120	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	NB	0.3273	-0.45	Poisson	0.9970	0.25	NB	0.0001	-4.75
182255	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	NB	0.0382	14.02	ZINB	0.0000	20.42	ZINB	0.9923	20.92
4401580	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	NB	0.0000	145.35	NB	0.0001	147.75	NB	0.0001	148.92
132041	Actinobacteria	Actinobacteria	Bifidobacteriales	Bifidobacteriaceae	Bifidobacterium	Poisson	0.9967	-0.20	NA	NA	NA	Poisson	0.9977	-1.00
905211	Actinobacteria	Actinobacteria	Actinomycetales	Micrococcaceae	Rothia	Poisson	0.9967	-0.20	NA	NA	NA	Poisson	0.9977	-1.00
186997	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Blautia	NB	0.0330	-104.57	NB	0.0030	39.33	NB	0.0002	43.00
4357811	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	ZINB	0.0578	10.20	ZINB	0.0002	14.25	ZINB	0.9924	14.50
189356	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	NB	0.0012	-2.23	Poisson	0.7406	-0.08	Poisson	0.9974	0.17
New.CleanUp.ReferenceOTU60780	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Blautia	Poisson	0.9965	-0.60	NA	NA	NA	NA	NA	NA
1024529	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	unclassified	ZINB	0.9976	-1.10	Poisson	0.9962	-2.25	NA	NA	NA
2875735	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	NB	0.0039	2.58	NB	0.9978	3.08	NB	0.9970	3.08
182483	Firmicutes	Erysipelotrichi	Erysipelotrichales	Erysipelotrichaceae	[Eubacterium]	#N/A	NA	NA	ZINB	0.9861	-58.75	Poisson	0.9986	-0.33
293843	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	#N/A	NA	NA	Poisson	0.9963	-1.25	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU43219	Firmicutes	Clostridia	Clostridiales	unclassified	unclassified	Poisson	0.9967	-0.20	NA	NA	NA	Poisson	0.9986	-0.67
2119418	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	ZINB	0.0000	29.90	ZINB	0.0020	22.00	ZINB	0.4657	-767.33
365385	Actinobacteria	Actinobacteria	Bifidobacteriales	Bifidobacteriaceae	Bifidobacterium	ZINB	0.7113	-45.98	ZINB	0.0000	29.42	ZINB	0.0137	-804.08
248902	Firmicutes	Bacilli	Turicibacterales	Turicibacteraceae	Turicibacter	#N/A	NA	NA	Poisson	0.9977	-0.75	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU632	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	#N/A	NA	NA	Poisson	0.9977	-0.75	Poisson	0.9986	-0.33
189793	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	unclassified	NB	0.9965	-0.70	Poisson	0.9963	-1.50	NA	NA	NA
186918	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	ZINB	0.9974	-0.80	Poisson	0.9963	-1.50	NA	NA	NA
147969	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Ruminococcus	NB	0.0630	-466.73	NB	0.9975	49.67	NB	0.9978	49.67
2157225	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	unclassified	NB	0.9963	-2.10	NB	0.9976	-4.00	Poisson	0.9986	-0.33
312969	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	#N/A	NA	NA	NB	0.9976	-1.75	Poisson	0.9963	-1.33
193778	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	Poisson	0.0465	-0.62	Poisson	0.9982	0.08	Poisson	0.9975	0.08
4439603	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	NB	0.0188	-20.43	NB	0.3875	-10.58	NB	0.0000	-387.50
New.CleanUp.ReferenceOTU38622	Firmicutes	Erysipelotrichi	Erysipelotrichales	Erysipelotrichaceae	Catenibacterium	#N/A	NA	NA	Poisson	0.9964	-1.00	Poisson	0.9964	-1.00
New.CleanUp.ReferenceOTU6973	Actinobacteria	Actinobacteria	Bifidobacteriales	Bifidobacteriaceae	Bifidobacterium	#N/A	NA	NA	Poisson	0.9977	-0.75	Poisson	0.9977	-0.67
New.ReferenceOTU239	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	#N/A	NA	NA	Poisson	0.9963	-1.50	ZINB	0.9982	-1.67
4468234	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	ZINB	0.0001	11.50	ZINB	0.0000	16.50	ZINB	0.0013	16.50
2280817	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	#N/A	NA	NA	ZINB	0.9969	-3.00	ZINB	0.9971	-4.00
296442	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	#N/A	NA	NA	NB	0.9976	-1.75	ZINB	0.9971	-5.00
772515	Firmicutes	Bacilli	Lactobacillales	Enterococcaceae	Enterococcus	#N/A	NA	NA	ZINB	0.9977	-2.00	ZINB	0.9923	-27.00
4409280	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	NB	0.0000	-138.12	NB	0.0000	-75.17	Poisson	0.0314	-0.92

271159	Firmicutes	Bacilli	Lactobacillales	unclassified	unclassified	Poisson	0.0320	-1.23	Poisson	0.0657	-1.33	NB	0.0000	-14.83
New.CleanUp.ReferenceOTU47595	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	Poisson	0.9968	0.75	Poisson	0.2973	0.50	Poisson	0.9972	0.75
New.CleanUp.ReferenceOTU42397	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	Poisson	0.9968	0.58	Poisson	0.9968	0.58	Poisson	0.9972	0.58
258375	Firmicutes	Clostridia	Clostridiales	Veillonellaceae	Dialister	Poisson	0.9981	0.08	Poisson	0.0571	-0.67	ZINB	0.0003	-4.58
186732	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Blautia	NB	0.0243	-746.32	NB	0.0120	206.08	NB	0.0074	216.75
3588390	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	ZINB	0.1123	243.63	ZINB	0.0000	443.08	ZINB	0.0000	449.83
New.CleanUp.ReferenceOTU38243	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	Poisson	0.9970	0.17	Poisson	0.9970	0.17	Poisson	0.0059	-1.50
4367187	Firmicutes	Clostridia	Clostridiales	Peptostreptococcaceae	unclassified	NB	0.8809	-0.27	NB	0.0055	-34.92	NB	0.9982	1.33
73471	Actinobacteria	Actinobacteria	Actinomycetales	Actinomycetaceae	Actinomyces	Poisson	0.9967	-0.20	NA	NA	NA	Poisson	0.9977	-1.00
4463108	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	NB	0.0000	-131.93	Poisson	0.0994	-0.58	NB	0.0000	-1663.50
2318497	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	unclassified	NB	0.0001	-46.23	NB	0.0000	-85.83	NB	0.1596	-9.17
584109	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	Poisson	0.9981	0.08	Poisson	0.1435	-0.42	Poisson	0.0062	-1.58
300297	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Coprococcus	ZINB	0.0000	-12.03	NB	0.0921	-34.33	ZINB	0.9958	1.17
New.CleanUp.ReferenceOTU51033	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Coprococcus	NB	0.0071	-7.67	ZINB	0.9971	0.33	ZINB	0.9975	0.33
557978	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	ZINB	0.9974	-1.00	NA	NA	NA	Poisson	0.9962	-3.33
370225	Actinobacteria	Actinobacteria	Bifidobacteriales	Bifidobacteriaceae	Bifidobacterium	Poisson	0.9981	0.08	Poisson	0.1435	-0.42	Poisson	0.0131	-1.25
369014	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	NB	0.0612	8.00	NB	0.0044	12.25	NB	0.0020	13.67
4411875	Actinobacteria	Actinobacteria	Bifidobacteriales	Bifidobacteriaceae	Scardovia	Poisson	0.9967	-0.20	NA	NA	NA	Poisson	0.9986	-0.67
4425512	Firmicutes	Clostridia	Clostridiales	Veillonellaceae	Veillonella	Poisson	0.9981	0.08	Poisson	0.4373	-0.17	Poisson	0.0314	-0.92
192383	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Ruminococcus	NB	0.4936	-3.83	NB	0.9978	4.67	NB	0.2085	4.33
4434334	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	unclassified	NB	0.6540	34.28	NB	0.0198	-701.42	NB	0.0002	140.25
231952	Firmicutes	Clostridia	Clostridiales	Christensenellaceae	unclassified	Poisson	0.9943	-1.10	Poisson	0.9978	-0.50	NA	NA	NA
4380191	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	Poisson	0.9949	0.67	NB	0.1748	-1.33	Poisson	0.9957	0.67
212532	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	NB	0.0003	-8.42	NB	0.0183	-2.42	Poisson	0.9975	0.08
3439403	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	ZINB	0.1519	23.93	ZINB	0.0000	43.08	ZINB	0.0000	44.17
4474255	Proteobacteria	Betaproteobacteria	Burkholderiales	Alcaligenaceae	Sutterella	Poisson	0.9943	-1.30	NA	NA	NA	Poisson	0.9977	-0.67
168071	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	ZINB	0.9969	-2.50	ZINB	0.9968	-4.50	NA	NA	NA
195651	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	NB	0.0160	21.75	NB	0.0053	29.00	NB	0.0000	35.25
191718	Firmicutes	Erysipelotrichi	Erysipelotrichales	Erysipelotrichaceae	unclassified	NB	0.0081	-1.53	Poisson	0.0017	-1.83	Poisson	0.9974	0.17
300662	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	unclassified	NB	0.0589	-2.53	ZINB	0.0000	-7.58	Poisson	0.9974	0.17
4396656	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	unclassified	NB	0.9962	-2.30	Poisson	0.9963	-1.50	NA	NA	NA
302160	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	ZINB	0.9949	-5.70	ZINB	0.9968	-4.75	NA	NA	NA
575768	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	unclassified	ZINB	0.9951	-3.80	ZINB	0.9969	-3.00	NA	NA	NA
177040	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Blautia	NB	0.2423	-20.12	NB	0.0064	20.58	NB	0.0106	21.08
593422	Firmicutes	Clostridia	Clostridiales	unclassified	unclassified	Poisson	0.0984	-0.57	NB	0.0010	-8.67	NB	0.9973	0.33
New.CleanUp.ReferenceOTU5616	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Anaerostipes	NB	0.6382	0.40	NB	0.9966	2.00	NB	0.9971	2.00

4466616	Proteobacteria	Gammaproteobacteria	Pasteurellales	Pasteurellaceae	Haemophilus	Poisson	0.9980	-0.10	Poisson	0.9979	-0.25	Poisson	0.9986	-0.67
2442706	Firmicutes	Clostridia	Clostridiales	Christensenellaceae	unclassified	NB	0.6309	2.83	NB	0.1633	7.33	ZINB	0.9886	7.83
4469576	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	NB	0.0582	36.98	NB	0.2446	33.83	NB	0.9966	58.08
4390319	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	NB	0.0412	32.97	NB	0.0003	37.92	NB	0.1147	32.00
185570	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	[Ruminococcus]	NB	0.9913	0.10	NB	0.9977	12.00	NB	0.9968	12.00
New.CleanUp.ReferenceOTU14075	Actinobacteria	Coriobacteriia	Coriobacteriales	Coriobacteriaceae	Collinsella	Poisson	0.9970	0.17	Poisson	0.9970	0.17	Poisson	0.1657	-0.50
1919007	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	NB	0.0460	4.35	NB	0.0039	6.50	NB	0.0139	6.08
1142029	Actinobacteria	Actinobacteria	Bifidobacteriales	Bifidobacteriaceae	Bifidobacterium	NB	0.0971	-29.22	NB	0.9444	0.83	NB	0.0019	-288.58
174614	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Ruminococcus	NB	0.0031	-9.00	NB	0.1017	-9.25	NB	0.9982	1.50
16054	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Ruminococcus	NB	0.0000	-115.27	ZINB	0.0000	-264.92	Poisson	0.9958	0.33
186888	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	NB	0.6136	1.98	NB	0.0141	7.83	NB	0.9969	8.58
4278525	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	NB	0.0144	13.72	NB	0.0023	17.17	NB	0.9968	17.42
230578	Actinobacteria	Coriobacteriia	Coriobacteriales	Coriobacteriaceae	unclassified	ZINB	0.9967	-1.50	ZINB	0.9947	-19.75	NA	NA	NA
New.CleanUp.ReferenceOTU53539	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	Poisson	0.9980	-0.10	Poisson	0.9963	-1.25	NA	NA	NA
327209	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	Poisson	0.9980	-0.10	ZINB	0.9969	-3.75	NA	NA	NA
New.CleanUp.ReferenceOTU30436	Firmicutes	Clostridia	Clostridiales	unclassified	unclassified	Poisson	0.9980	-0.10	Poisson	0.9963	-1.75	NA	NA	NA
176077	Firmicutes	Clostridia	Clostridiales	unclassified	unclassified	ZINB	0.4413	0.15	ZINB	0.0015	-0.25	ZINB	0.9959	0.75
182033	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Oscillospira	NB	0.5747	-0.80	NB	0.9979	1.50	NB	0.9982	1.50
4428313	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	ZINB	0.9870	5.33	ZINB	0.9918	5.33	NB	0.6194	-13.33
182643	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	unclassified	NB	0.1058	-13.50	NB	0.0038	-73.50	NB	0.9981	2.00
4304475	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	Poisson	0.0654	0.63	Poisson	0.9968	0.83	Poisson	0.9956	0.83
191601	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Blautia	Poisson	0.0101	1.82	NB	0.4610	1.17	Poisson	0.9953	3.42
183496	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	NB	0.0069	2.87	NB	0.9978	3.17	NB	0.9970	3.17
1010113	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	ZINB	0.9784	-371.00
4339160	Firmicutes	Bacilli	Lactobacillales	Enterococcaceae	unclassified	#N/A	NA	NA	NA	NA	NA	ZINB	0.9788	-272.67
New.CleanUp.ReferenceOTU55872	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	ZINB	0.9802	-143.67
537290	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Morganella	#N/A	NA	NA	NA	NA	NA	ZINB	0.9872	-76.33
225919	Firmicutes	Bacilli	Lactobacillales	unclassified	unclassified	#N/A	NA	NA	NA	NA	NA	ZINB	0.9874	-65.33
185593	Tenericutes	Mollicutes	Anaeroplasmatales	Anaeroplasmataceae	unclassified	#N/A	NA	NA	NA	NA	NA	ZINB	0.9921	-41.67
4338745	Firmicutes	Clostridia	Clostridiales	Veillonellaceae	unclassified	#N/A	NA	NA	NA	NA	NA	ZINB	0.9922	-28.67
New.CleanUp.ReferenceOTU45318	Firmicutes	Bacilli	Lactobacillales	Enterococcaceae	Enterococcus	#N/A	NA	NA	NA	NA	NA	ZINB	0.9922	-28.33
New.CleanUp.ReferenceOTU29026	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	ZINB	0.9922	-29.00
New.CleanUp.ReferenceOTU61682	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Lactococcus	#N/A	NA	NA	NA	NA	NA	ZINB	0.9923	-23.33
300829	Firmicutes	Clostridia	Clostridiales	Veillonellaceae	Dialister	#N/A	NA	NA	NA	NA	NA	ZINB	0.9924	-38.67

131660	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	ZINB	0.9927	-29.33
831342	Actinobacteria	Actinobacteria	Bifidobacteriales	Bifidobacteriaceae	Bifidobacterium	#N/A	NA	NA	NA	NA	NA	ZINB	0.9951	-18.67
112026	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	ZINB	0.9952	-17.00
114166	Firmicutes	Bacilli	Lactobacillales	Enterococcaceae	Enterococcus	#N/A	NA	NA	NA	NA	NA	ZINB	0.9952	-16.00
329096	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	ZINB	0.9952	-14.00
4354311	Firmicutes	Bacilli	Lactobacillales	Enterococcaceae	Enterococcus	#N/A	NA	NA	NA	NA	NA	ZINB	0.9952	-14.00
New.CleanUp.ReferenceOTU60885	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	ZINB	0.9952	-13.00
266445	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	ZINB	0.9952	-12.33
810831	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	ZINB	0.9952	-12.00
1138534	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	ZINB	0.9953	-11.00
851794	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	ZINB	0.9953	-10.00
746679	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	ZINB	0.9953	-9.00
4343005	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Erwinia	#N/A	NA	NA	NA	NA	NA	ZINB	0.9953	-9.00
New.CleanUp.ReferenceOTU1306	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	ZINB	0.9953	-8.67
New.CleanUp.ReferenceOTU62748	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	ZINB	0.9954	-7.33
329693	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	#N/A	NA	NA	NA	NA	NA	Poisson	0.9963	-1.33
537734	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9963	-1.33
809106	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9963	-1.33
1108706	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9963	-1.33
1888072	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9963	-1.33
4418165	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9963	-1.33
New.CleanUp.ReferenceOTU26906	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9963	-1.33
New.CleanUp.ReferenceOTU30213	Firmicutes	Bacilli	Lactobacillales	Enterococcaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9963	-1.33
New.CleanUp.ReferenceOTU40192	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9963	-1.33
New.CleanUp.ReferenceOTU58445	Actinobacteria	Actinobacteria	Bifidobacteriales	Bifidobacteriaceae	Bifidobacterium	#N/A	NA	NA	NA	NA	NA	Poisson	0.9963	-1.33
New.ReferenceOTU384	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9963	-1.33
New.CleanUp.ReferenceOTU49927	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Lactococcus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9963	-1.33
10085	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9964	-1.00
162335	Firmicutes	Bacilli	Lactobacillales	unclassified	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9964	-1.00
305982	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9964	-1.00
544824	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Trabulsiella	#N/A	NA	NA	NA	NA	NA	Poisson	0.9964	-1.00
810399	Firmicutes	Bacilli	Lactobacillales	Enterococcaceae	Enterococcus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9964	-1.00
886735	Firmicutes	Bacilli	Lactobacillales	Aerococcaceae	Alloiococcus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9964	-1.00

1119540	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9964	-1.00
4318990	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Erwinia	#N/A	NA	NA	NA	NA	NA	Poisson	0.9964	-1.00
4399988	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9964	-1.00
4416562	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9964	-1.00
New.CleanUp.ReferenceOTU23455	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9964	-1.00
New.CleanUp.ReferenceOTU24389	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9964	-1.00
New.CleanUp.ReferenceOTU2755	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9964	-1.00
New.CleanUp.ReferenceOTU27811	Firmicutes	Erysipelotrichi	Erysipelotrichales	Erysipelotrichaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9964	-1.00
New.CleanUp.ReferenceOTU30619	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9964	-1.00
New.CleanUp.ReferenceOTU40266	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9964	-1.00
New.CleanUp.ReferenceOTU41246	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Morganella	#N/A	NA	NA	NA	NA	NA	Poisson	0.9964	-1.00
New.CleanUp.ReferenceOTU49391	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9964	-1.00
New.CleanUp.ReferenceOTU51325	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9964	-1.00
New.CleanUp.ReferenceOTU57794	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9964	-1.00
New.CleanUp.ReferenceOTU60590	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Roseburia	#N/A	NA	NA	NA	NA	NA	Poisson	0.9964	-1.00
295194	Firmicutes	Erysipelotrichi	Erysipelotrichales	Erysipelotrichaceae	Catenibacterium	#N/A	NA	NA	NA	NA	NA	Poisson	0.9964	-1.00
3101394	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9964	-1.00
New.CleanUp.ReferenceOTU36132	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9964	-1.00
New.CleanUp.ReferenceOTU54597	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9964	-1.00
2749362	Firmicutes	Bacilli	Lactobacillales	Enterococcaceae	unclassified	#N/A	NA	NA	NA	NA	NA	ZINB	0.9971	-6.00
586387	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Lactococcus	#N/A	NA	NA	NA	NA	NA	ZINB	0.9971	-5.00
2951780	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	#N/A	NA	NA	NA	NA	NA	ZINB	0.9971	-5.00
New.CleanUp.ReferenceOTU48258	Firmicutes	Bacilli	Lactobacillales	Enterococcaceae	unclassified	#N/A	NA	NA	NA	NA	NA	ZINB	0.9971	-4.33
149335	Firmicutes	Clostridia	Clostridiales	Veillonellaceae	Mitsuokella	#N/A	NA	NA	NA	NA	NA	ZINB	0.9971	-4.00
328727	Firmicutes	Bacilli	Lactobacillales	unclassified	unclassified	#N/A	NA	NA	NA	NA	NA	ZINB	0.9972	-3.00
4376230	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	ZINB	0.9972	-3.00
New.CleanUp.ReferenceOTU32922	Firmicutes	Bacilli	Lactobacillales	Enterococcaceae	Enterococcus	#N/A	NA	NA	NA	NA	NA	ZINB	0.9972	-3.00
New.CleanUp.ReferenceOTU4	Actinobacteria	Actinobacteria	Bifidobacteriales	Bifidobacteriaceae	Bifidobacterium	#N/A	NA	NA	NA	NA	NA	ZINB	0.9972	-3.00

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New.CleanUp.ReferenceOTU51046	Firmicutes	Bacilli	Lactobacillales	Enterococcaceae	Enterococcus	#N/A	NA	NA	NA	NA	NA	ZINB	0.9972	-3.00
839152	Firmicutes	Bacilli	Lactobacillales	Enterococcaceae	unclassified	#N/A	NA	NA	NA	NA	NA	ZINB	0.9972	-2.67
New.CleanUp.ReferenceOTU57244	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	ZINB	0.9972	-2.67
New.CleanUp.ReferenceOTU47023	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	ZINB	0.9974	-3.67
898207	Firmicutes	Bacilli	Lactobacillales	unclassified	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
1015518	Actinobacteria	Actinobacteria	Actinomycetales	Corynebacteriaceae	Corynebacterium	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
4322712	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
4397962	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
4437024	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU12331	Firmicutes	Clostridia	Clostridiales	Veillonellaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU14248	Firmicutes	Clostridia	Clostridiales	unclassified	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU18257	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Lactococcus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU2445	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Lactococcus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU26397	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Lachnospira	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU29124	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU32556	unclassified	unclassified	unclassified	unclassified	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU40006	unclassified	unclassified	unclassified	unclassified	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU41478	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU42414	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU42491	Firmicutes	Erysipelotrichi	Erysipelotrichales	Erysipelotrichaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU43573	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU43819	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Roseburia	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU47378	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU55727	Firmicutes	Clostridia	Clostridiales	Veillonellaceae	Mitsuokella	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.Refer	Firmicutes	Clostridia	Clostridiales	Veillonellaceae	Megasphaera	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67

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New.CleanUp.ReferenceOTU61510	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU62060	Actinobacteria	Actinobacteria	Actinomycetales	Micrococcaceae	Rothia	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU9756	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
106985	Proteobacteria	Gammaproteobacteria	Pseudomonadales	Pseudomonadaceae	Pseudomonas	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
180825	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU13062	Firmicutes	Bacilli	Turicibacterales	Turicibacteraceae	Turicibacter	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU21035	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU23967	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Faecalibacterium	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU26957	Actinobacteria	Actinobacteria	Bifidobacteriales	Bifidobacteriaceae	Bifidobacterium	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU30079	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU30203	Firmicutes	Bacilli	Turicibacterales	Turicibacteraceae	Turicibacter	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU33065	Firmicutes	Clostridia	Clostridiales	Veillonellaceae	Dialister	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU41194	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU54826	Firmicutes	Clostridia	Clostridiales	unclassified	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU58059	Firmicutes	Clostridia	Clostridiales	Veillonellaceae	Dialister	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU62969	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU63987	Actinobacteria	Actinobacteria	Bifidobacteriales	Bifidobacteriaceae	Bifidobacterium	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
99882	Firmicutes	Bacilli	Lactobacillales	Enterococcaceae	Enterococcus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
132873	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
134671	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
368849	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
956702	Proteobacteria	Gammaproteobacteria	Pasteurellales	Pasteurellaceae	Haemophilus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
4415598	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
4418243	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
4454257	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU10419	Firmicutes	Bacilli	Lactobacillales	Enterococcaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67

New.CleanUp.ReferenceOTU13221	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU13907	Actinobacteria	Actinobacteria	Bifidobacteriales	Bifidobacteriaceae	Bifidobacterium	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU14322	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU15095	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU16820	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU23594	Proteobacteria	unclassified	unclassified	unclassified	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU23714	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Proteus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU24605	Firmicutes	Bacilli	Lactobacillales	Enterococcaceae	Enterococcus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU24978	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU25361	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU27883	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU28027	unclassified	unclassified	unclassified	unclassified	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU30058	Firmicutes	Bacilli	Lactobacillales	Enterococcaceae	Enterococcus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU38312	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU40200	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU4239	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU42391	Actinobacteria	Actinobacteria	Bifidobacteriales	Bifidobacteriaceae	Bifidobacterium	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU43802	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU45286	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU4675	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU51121	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU54598	Firmicutes	Bacilli	Lactobacillales	Enterococcaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.Refer	Firmicutes	Bacilli	Lactobacillales	Enterococcaceae	Enterococcus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67

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New.CleanUp.ReferenceOTU56297	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU58817	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Morganella	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU62160	Firmicutes	Bacilli	Lactobacillales	unclassified	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU63065	Firmicutes	Bacilli	Lactobacillales	unclassified	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU6625	Firmicutes	Bacilli	Lactobacillales	Enterococcaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU705	Firmicutes	Bacilli	Lactobacillales	unclassified	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU891	Firmicutes	Bacilli	Lactobacillales	Enterococcaceae	Enterococcus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
New.CleanUp.ReferenceOTU9420	Proteobacteria	Betaproteobacteria	Burkholderiales	Alcaligenaceae	Sutterella	#N/A	NA	NA	NA	NA	NA	Poisson	0.9977	-0.67
146935	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	ZINB	0.9982	-2.33
524674	Firmicutes	Bacilli	Lactobacillales	Enterococcaceae	Enterococcus	#N/A	NA	NA	NA	NA	NA	ZINB	0.9982	-2.33
1055212	Firmicutes	Bacilli	Lactobacillales	Enterococcaceae	Enterococcus	#N/A	NA	NA	NA	NA	NA	ZINB	0.9982	-2.33
1722623	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	ZINB	0.9982	-2.33
4362942	Firmicutes	Bacilli	Lactobacillales	Enterococcaceae	Enterococcus	#N/A	NA	NA	NA	NA	NA	ZINB	0.9982	-2.33
New.CleanUp.ReferenceOTU23328	Firmicutes	Bacilli	Lactobacillales	Enterococcaceae	Enterococcus	#N/A	NA	NA	NA	NA	NA	ZINB	0.9982	-2.33
New.CleanUp.ReferenceOTU57129	Firmicutes	Bacilli	Lactobacillales	Enterococcaceae	unclassified	#N/A	NA	NA	NA	NA	NA	ZINB	0.9982	-2.33
New.CleanUp.ReferenceOTU61044	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Lactococcus	#N/A	NA	NA	NA	NA	NA	ZINB	0.9982	-2.00
85614	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Morganella	#N/A	NA	NA	NA	NA	NA	ZINB	0.9982	-2.00
366451	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	ZINB	0.9982	-2.00
624891	Firmicutes	Bacilli	Lactobacillales	Enterococcaceae	Enterococcus	#N/A	NA	NA	NA	NA	NA	ZINB	0.9982	-2.00
829186	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	ZINB	0.9982	-2.00
New.CleanUp.ReferenceOTU34672	Firmicutes	Bacilli	Lactobacillales	unclassified	unclassified	#N/A	NA	NA	NA	NA	NA	ZINB	0.9982	-2.00
New.CleanUp.ReferenceOTU7000	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Morganella	#N/A	NA	NA	NA	NA	NA	ZINB	0.9982	-2.00
4328189	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Serratia	#N/A	NA	NA	NA	NA	NA	ZINB	0.9982	-1.67
210965	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	[Ruminococcus]	#N/A	NA	NA	NA	NA	NA	ZINB	0.9985	-1.67
239362	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	ZINB	0.9985	-1.67
3441309	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	ZINB	0.9985	-1.67
4359590	Firmicutes	Bacilli	Lactobacillales	Enterococcaceae	unclassified	#N/A	NA	NA	NA	NA	NA	ZINB	0.9985	-1.67
4379242	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	ZINB	0.9985	-1.67
4475784	Firmicutes	Bacilli	Lactobacillales	Enterococcaceae	Enterococcus	#N/A	NA	NA	NA	NA	NA	ZINB	0.9985	-1.67

New.CleanUp.ReferenceOTU38895	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	ZINB	0.9985	-1.67
New.CleanUp.ReferenceOTU44732	Firmicutes	Bacilli	Lactobacillales	Enterococcaceae	Enterococcus	#N/A	NA	NA	NA	NA	NA	ZINB	0.9985	-1.67
26608	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
91962	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
292364	Firmicutes	Bacilli	Lactobacillales	Enterococcaceae	Enterococcus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
318764	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
637546	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
718624	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
836776	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
837075	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
997439	Actinobacteria	Actinobacteria	Bifidobacteriales	Bifidobacteriaceae	Bifidobacterium	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
1065569	Firmicutes	Bacilli	Lactobacillales	Aerococcaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
1071929	Firmicutes	Bacilli	Gemellales	Gemellaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
1116674	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
1129680	Firmicutes	Bacilli	Lactobacillales	unclassified	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
1135616	Firmicutes	Bacilli	Lactobacillales	Enterococcaceae	Enterococcus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
2281837	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
3355047	Firmicutes	Bacilli	Lactobacillales	Enterococcaceae	Enterococcus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
3440955	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Proteus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
4297549	Firmicutes	Bacilli	Lactobacillales	Enterococcaceae	Enterococcus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
4338372	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
4348151	Firmicutes	Bacilli	Lactobacillales	Enterococcaceae	Enterococcus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
4440251	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
4447432	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
4478762	Firmicutes	Bacilli	Lactobacillales	unclassified	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU10680	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU10926	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU11802	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Morganella	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU11804	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU13931	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU1492	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU15911	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.Refer	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33

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New.CleanUp.ReferenceOTU16164	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU17106	Firmicutes	Bacilli	Lactobacillales	Enterococcaceae	Enterococcus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU18640	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU18893	Firmicutes	Bacilli	Lactobacillales	unclassified	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU20455	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU21395	Firmicutes	Bacilli	Lactobacillales	Enterococcaceae	Enterococcus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU23118	Firmicutes	Bacilli	Lactobacillales	Enterococcaceae	Enterococcus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU24785	Actinobacteria	Actinobacteria	Bifidobacteriales	Bifidobacteriaceae	Bifidobacterium	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU26999	unclassified	unclassified	unclassified	unclassified	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU27006	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU28984	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU29878	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Proteus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU31000	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU33308	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU33789	Firmicutes	Bacilli	Lactobacillales	unclassified	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU35236	Firmicutes	Bacilli	Lactobacillales	unclassified	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU37750	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU38144	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU399	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU41930	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU42682	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU44359	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33

New.CleanUp.ReferenceOTU47480	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU47920	unclassified	unclassified	unclassified	unclassified	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU48129	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU49949	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	Morganella	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU53115	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU53654	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU5463	Firmicutes	Bacilli	Lactobacillales	Enterococcaceae	Enterococcus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU54972	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU55211	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU5643	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU56600	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU58117	Actinobacteria	Actinobacteria	Bifidobacteriales	Bifidobacteriaceae	Bifidobacterium	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU59667	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU603	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU63921	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU7090	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU7152	unclassified	unclassified	unclassified	unclassified	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU8016	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU9289	unclassified	unclassified	unclassified	unclassified	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU9533	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
169428	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
189674	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
190107	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
194626	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Faecalibacterium	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33

215670	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
463794	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
517754	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
518002	Proteobacteria	Gammaproteobacteria	Enterobacteriales	Enterobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
824876	Actinobacteria	Actinobacteria	Bifidobacteriales	Bifidobacteriaceae	Bifidobacterium	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
865469	Proteobacteria	Gammaproteobacteria	Pasteurellales	Pasteurellaceae	Haemophilus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
923098	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
1062051	Actinobacteria	Actinobacteria	Actinomycetales	Corynebacteriaceae	Corynebacterium	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
1086274	Proteobacteria	Gammaproteobacteria	Pasteurellales	Pasteurellaceae	Haemophilus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
1523543	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Lactococcus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
1918929	Proteobacteria	Alphaproteobacteria	Rickettsiales	mitochondria	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
2750316	Firmicutes	Erysipelotrichi	Erysipelotrichales	Erysipelotrichaceae	Catenibacterium	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
4315660	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Lactococcus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
4341056	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
4367364	Firmicutes	Bacilli	Gemellales	Gemellaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
4393181	Tenericutes	Mollicutes	Mycoplasmatales	Mycoplasmataceae	Mycoplasma	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
4447605	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
4447992	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
4467992	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU10424	Firmicutes	Erysipelotrichi	Erysipelotrichales	Erysipelotrichaceae	Catenibacterium	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU10629	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU10740	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU13525	Actinobacteria	Actinobacteria	Bifidobacteriales	Bifidobacteriaceae	Bifidobacterium	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU13660	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Lachnospira	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU13987	Firmicutes	Clostridia	Clostridiales	Veillonellaceae	Dialister	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU1438	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU14929	Firmicutes	Clostridia	Clostridiales	Veillonellaceae	Veillonella	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU16846	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Lachnospira	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU16922	Firmicutes	Clostridia	Clostridiales	unclassified	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU17818	Actinobacteria	Actinobacteria	Bifidobacteriales	Bifidobacteriaceae	Bifidobacterium	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU1	Actinobacteria	Coriobacteriia	Coriobacteriales	Coriobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33

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New.CleanUp.ReferenceOTU18086	Firmicutes	Clostridia	Clostridiales	Veillonellaceae	Dialister	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU18132	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU20420	Actinobacteria	Coriobacteriia	Coriobacteriales	Coriobacteriaceae	Collinsella	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU21019	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Lactococcus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU22110	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU24231	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU24236	Actinobacteria	Coriobacteriia	Coriobacteriales	Coriobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU24362	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU25916	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Roseburia	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU28349	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU28440	Firmicutes	Erysipelotrichi	Erysipelotrichales	Erysipelotrichaceae	Catenibacterium	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU29562	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU29783	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU29817	unclassified	unclassified	unclassified	unclassified	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU30038	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU30791	Actinobacteria	Coriobacteriia	Coriobacteriales	Coriobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU30837	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Roseburia	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU3206	Firmicutes	Erysipelotrichi	Erysipelotrichales	Erysipelotrichaceae	Catenibacterium	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU32256	Firmicutes	Erysipelotrichi	Erysipelotrichales	Erysipelotrichaceae	Catenibacterium	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU32629	Firmicutes	Clostridia	Clostridiales	unclassified	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU33956	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU35858	unclassified	unclassified	unclassified	unclassified	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33

New.CleanUp.ReferenceOTU35948	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU3657	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU38077	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU38417	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Lachnospira	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU39803	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU39849	Firmicutes	Clostridia	Clostridiales	unclassified	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU3995	Actinobacteria	Coriobacteriia	Coriobacteriales	Coriobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU40792	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Lactococcus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU41394	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU42302	Actinobacteria	Coriobacteriia	Coriobacteriales	Coriobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU42660	Actinobacteria	Actinobacteria	Actinomycetales	Micrococcaceae	Rothia	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU43708	Actinobacteria	Coriobacteriia	Coriobacteriales	Coriobacteriaceae	Eggerthella	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU44468	Firmicutes	Erysipelotrichi	Erysipelotrichales	Erysipelotrichaceae	Catenibacterium	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU44532	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU4545	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU46653	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU47812	Firmicutes	Clostridia	Clostridiales	Veillonellaceae	Megasphaera	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU47937	Firmicutes	Clostridia	Clostridiales	Veillonellaceae	Veillonella	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU50178	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU50688	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU50814	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Faecalibacterium	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU53386	Actinobacteria	Coriobacteriia	Coriobacteriales	Coriobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.Refer	Firmicutes	Clostridia	Clostridiales	Veillonellaceae	Megasphaera	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33

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New.CleanUp.ReferenceOTU56421	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU56690	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU56979	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Moryella	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU57554	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	Clostridium	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU59237	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU60076	Firmicutes	Clostridia	Clostridiales	Veillonellaceae	Mitsuokella	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU60621	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Roseburia	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU61264	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Lactococcus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU62076	Actinobacteria	Actinobacteria	Bifidobacteriales	Bifidobacteriaceae	Bifidobacterium	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU63301	Actinobacteria	Actinobacteria	Actinomycetales	Micrococcaceae	Rothia	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU6408	Firmicutes	Bacilli	Lactobacillales	Lactobacillaceae	Lactobacillus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU682	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Lactococcus	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU6847	Firmicutes	Erysipelotrichi	Erysipelotrichales	Erysipelotrichaceae	Catenibacterium	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU6863	Firmicutes	Clostridia	Clostridiales	Veillonellaceae	Mitsuokella	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU7425	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU7447	Actinobacteria	Actinobacteria	Bifidobacteriales	Bifidobacteriaceae	Bifidobacterium	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU823	Actinobacteria	Coriobacteriia	Coriobacteriales	Coriobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
New.CleanUp.ReferenceOTU904	Firmicutes	Clostridia	Clostridiales	Veillonellaceae	Mitsuokella	#N/A	NA	NA	NA	NA	NA	Poisson	0.9986	-0.33
4328026	Actinobacteria	Coriobacteriia	Coriobacteriales	Coriobacteriaceae	unclassified	#N/A	NA	NA	NA	NA	NA	ZINB	0.9990	-54.33
847934	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	Poisson	0.0081	-1.22	Poisson	0.9982	0.08	Poisson	0.9975	0.08
681370	Actinobacteria	Actinobacteria	Bifidobacteriales	Bifidobacteriaceae	Bifidobacterium	NB	0.3196	-22.20	NB	0.0026	33.75	NB	0.0970	-99.33
New.CleanUp.ReferenceOTU35138	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	Poisson	0.0229	1.02	Poisson	0.9967	1.42	Poisson	0.5781	0.42
591439	Firmicutes	Clostridia	Clostridiales	[Mogibacteriaceae]	unclassified	ZINB	0.9961	-1.70	NA	NA	NA	Poisson	0.9976	-1.67
2272791	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	unclassified	ZINB	0.0000	-5.23	NB	0.0001	-6.83	Poisson	0.0163	-1.17

180216	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	ZINB	0.0555	30.78	NB	0.0051	35.83	NB	0.9966	37.58
526682	Actinobacteria	Actinobacteria	Actinomycetales	Actinomycetaceae	Actinomyces	Poisson	0.0049	-1.23	Poisson	0.9970	0.17	Poisson	0.1657	-0.50
New.CleanUp.ReferenceOTU8720	Firmicutes	Clostridia	Clostridiales	unclassified	unclassified	Poisson	0.9980	-0.10	Poisson	0.9977	-0.75	NA	NA	NA
New.CleanUp.ReferenceOTU20860	Firmicutes	Erysipelotrichi	Erysipelotrichales	Erysipelotrichaceae	unclassified	Poisson	0.9980	-0.10	Poisson	0.9977	-0.75	NA	NA	NA
4332078	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	unclassified	Poisson	0.9980	-0.10	Poisson	0.9964	-1.00	NA	NA	NA
New.CleanUp.ReferenceOTU42900	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Lachnospira	Poisson	0.9980	-0.10	Poisson	0.9977	-0.75	NA	NA	NA
New.CleanUp.ReferenceOTU48210	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	Poisson	0.9980	-0.10	Poisson	0.9977	-0.75	NA	NA	NA
New.CleanUp.ReferenceOTU37518	Firmicutes	Clostridia	Clostridiales	unclassified	unclassified	NB	0.9963	-1.30	NA	NA	NA	NA	NA	NA
New.CleanUp.ReferenceOTU38464	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Ruminococcus	NB	0.9964	-0.90	NA	NA	NA	NA	NA	NA
320627	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	ZINB	0.9943	-2.80	NA	NA	NA	NA	NA	NA
367814	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Anaerotruncus	ZINB	0.9945	-1.80	NA	NA	NA	NA	NA	NA
296872	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	ZINB	0.9952	-2.70	NA	NA	NA	NA	NA	NA
178712	Firmicutes	Clostridia	Clostridiales	unclassified	unclassified	NB	0.9976	-3.40	NA	NA	NA	NA	NA	NA
New.CleanUp.ReferenceOTU34585	Actinobacteria	Actinobacteria	Bifidobacteriales	Bifidobacteriaceae	Bifidobacterium	Poisson	0.8974	-0.02	Poisson	0.9982	0.08	Poisson	0.0314	-0.92
930592	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	Poisson	0.8974	-0.02	Poisson	0.9982	0.08	Poisson	0.0314	-0.92
300620	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	ZINB	0.9873	-27.70	NA	NA	NA	NA	NA	NA
4372003	Bacteroidetes	Bacteroidia	Bacteroidales	Porphyromonadaceae	Parabacteroides	ZINB	0.9908	-5.80	NA	NA	NA	NA	NA	NA
190226	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Dorea	ZINB	0.9909	-4.40	NA	NA	NA	NA	NA	NA
360890	Firmicutes	Clostridia	Clostridiales	unclassified	unclassified	NB	0.0002	-41.23	Poisson	0.9970	0.17	Poisson	0.9974	0.17
349431	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Ruminococcus	NB	0.0029	-3.82	Poisson	0.9982	0.08	Poisson	0.9975	0.08
4449236	Proteobacteria	Betaproteobacteria	Burkholderiales	Alcaligenaceae	Sutterella	ZINB	0.1692	-187.87	ZINB	0.0007	52.83	ZINB	0.0635	-493.00
New.CleanUp.ReferenceOTU55964	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	Poisson	0.1207	0.53	Poisson	0.9968	0.83	Poisson	0.9956	0.83
188753	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Blautia	NB	0.0354	-20.18	NB	0.0566	6.42	NB	0.0169	7.75
4393532	Actinobacteria	Coriobacteriia	Coriobacteriales	Coriobacteriaceae	Eggerthella	NB	0.6231	-17.95	NB	0.0000	40.00	NB	0.0049	36.58
New.CleanUp.ReferenceOTU30629	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Ruminococcus	Poisson	0.9981	0.08	Poisson	0.0571	-0.67	Poisson	0.9975	0.08
192009	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	Poisson	0.0330	-0.72	Poisson	0.9982	0.08	Poisson	0.9975	0.08
216710	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	NB	0.9963	-2.10	ZINB	0.9957	-5.00	NA	NA	NA
New.CleanUp.ReferenceOTU47930	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	Poisson	0.9968	0.42	Poisson	0.9969	0.42	Poisson	0.9973	0.42
New.CleanUp.ReferenceOTU36140	Firmicutes	Clostridia	Clostridiales	unclassified	unclassified	Poisson	0.9967	-0.20	Poisson	0.9977	-1.00	NA	NA	NA
4360486	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	Poisson	0.9980	-0.10	Poisson	0.9978	-0.50	NA	NA	NA
New.CleanUp.ReferenceOTU1	Firmicutes	Clostridia	Clostridiales	unclassified	unclassified	Poisson	0.9980	-0.10	Poisson	0.9978	-0.50	NA	NA	NA

986														
New.CleanUp.ReferenceOTU46840	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	Poisson	0.9980	-0.10	Poisson	0.9978	-0.50	NA	NA	NA
695909	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	unclassified	Poisson	0.9980	-0.10	Poisson	0.9978	-0.50	NA	NA	NA
New.ReferenceOTU259	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	Poisson	0.9949	0.67	Poisson	0.9950	0.67	Poisson	0.9957	0.67
198696	Firmicutes	Clostridia	Clostridiales	unclassified	unclassified	Poisson	0.0207	-0.83	Poisson	0.7406	-0.08	Poisson	0.0023	-1.83
72820	Actinobacteria	Actinobacteria	Bifidobacteriales	Bifidobacteriaceae	Bifidobacterium	NB	0.3119	-1391.97	NB	0.0020	1667.08	NB	0.5251	-1285.33
New.CleanUp.ReferenceOTU45230	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	Poisson	0.9968	0.58	Poisson	0.9968	0.58	Poisson	0.9957	0.58
1102370	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	ZINB	0.9947	-3.10	ZINB	0.9914	-30.00	NA	NA	NA
New.CleanUp.ReferenceOTU29373	Bacteroidetes	Bacteroidia	Bacteroidales	Prevotellaceae	Prevotella	Poisson	0.9967	-0.20	Poisson	0.9963	-1.75	NA	NA	NA
New.CleanUp.ReferenceOTU63216	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	Poisson	0.9967	-0.20	Poisson	0.9964	-1.00	NA	NA	NA
194339	Firmicutes	Clostridia	Clostridiales	unclassified	unclassified	ZINB	0.9980	-0.90	ZINB	0.9947	-5.50	NA	NA	NA
4008675	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	Poisson	0.9949	0.67	Poisson	0.9950	0.67	Poisson	0.9957	0.67
258099	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	NB	0.6613	-1.00	NB	0.3396	2.00	NB	0.9981	2.50
4343184	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	Poisson	0.4275	0.15	Poisson	0.0695	-0.75	Poisson	0.9974	0.25
191483	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	NB	0.1431	3.00	NB	0.0099	5.25	NB	0.0237	5.17
4442130	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	NB	0.6839	-1.17	NB	0.9978	4.33	NB	0.0003	-85.33
190441	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	NB	0.7104	-0.63	NB	0.0201	2.92	NB	0.9970	3.17
New.CleanUp.ReferenceOTU64461	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	Poisson	0.0951	0.85	Poisson	0.9947	1.75	Poisson	0.9954	1.75
353336	Firmicutes	Clostridia	Clostridiales	unclassified	unclassified	Poisson	0.9981	0.08	Poisson	0.1435	-0.42	Poisson	0.9975	0.08
New.CleanUp.ReferenceOTU44280	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Blautia	Poisson	0.9981	0.08	Poisson	0.1435	-0.42	Poisson	0.9975	0.08
536866	Firmicutes	Bacilli	Lactobacillales	Streptococcaceae	Streptococcus	NB	0.0777	-6.17	NB	0.0370	2.58	NB	0.0000	-21.00
182196	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	unclassified	NB	0.8905	0.60	NB	0.0437	7.50	NB	0.0019	11.17
New.CleanUp.ReferenceOTU53780	Firmicutes	Clostridia	Clostridiales	unclassified	unclassified	NB	0.2196	-1.23	NB	0.0124	-2.83	Poisson	0.9974	0.17
2932557	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	Poisson	0.9967	-0.20	Poisson	0.9977	-0.75	NA	NA	NA
New.CleanUp.ReferenceOTU55696	Firmicutes	Erysipelotrichi	Erysipelotrichales	Erysipelotrichaceae	Catenibacterium	ZINB	0.9988	-0.30	Poisson	0.9964	-1.00	NA	NA	NA
4041792	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	unclassified	NB	0.0617	-1.12	Poisson	0.0075	-1.42	Poisson	0.9975	0.08
176297	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Roseburia	NB	0.1163	0.65	NB	0.4347	-0.75	NB	0.9972	0.75
194223	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Ruminococcus	Poisson	0.9965	-0.60	Poisson	0.9977	-0.75	NA	NA	NA
4321810	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Blautia	NB	0.7382	9.42	NB	0.0005	35.67	NB	0.9966	35.92
175836	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	unclassified	NB	0.0011	-10.37	ZINB	0.0047	-3.42	NB	0.9972	0.83
357046	Bacteroidetes	Bacteroidia	Bacteroidales	Rikenellaceae	unclassified	NB	0.1013	-480.98	NB	0.0005	120.92	NB	0.0022	121.08
4340358	Bacteroidetes	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	NB	0.0025	7.53	NB	0.9977	8.33	NB	0.2273	6.33
15728	Firmicutes	Erysipelotrichi	Erysipelotrichales	Erysipelotrichaceae	Holdemania	NB	0.6083	-3.80	ZINB	0.0005	10.50	NB	0.0100	11.33

Table S6. Significantly differential Fungal OTUs between UC-MCS. Profiled by Illumina paired-end sequencing of the ITS2 region. Table sorted by OTU. Linear mixed-effects regression models were applied to determine pairwise differences amongst UC-MCS (p-value<0.05).

OTU	Phylum	Class	Order	Family	Genus	MCS1-2 Model	MCS1-2 pvalue	MCS1-2 qvalue	MCS1-2 change	MCS1-3 Model	MCS1-3 pvalue	MCS1-3 qvalue	MCS1-3 change	MCS1-4 Model	MCS1-4 pvalue	MCS1-4 qvalue	MCS1-4 change
OTU_1	Ascomycota	Saccharomycetes	Saccharomycetales	Saccharomycetaceae	Saccharomyces	ZINB	0.5134	0.9988	-822.77	NB	0.0000	0.0000	-1340.17	NB	0.0000	0.0000	-1877.50
OTU_11	Ascomycota	Saccharomycetes	Saccharomycetales	Saccharomycetaceae	Kazachstania	ZINB	0.1142	0.9988	1.22	ZINB	0.0000	0.0000	-223.08	ZINB	0.2064	0.9986	-1575.92
OTU_123	Ascomycota	Eurotiomycetes	Eurotiales	Trichocomaceae	Aspergillus	Poisson	0.9970	0.9988	0.17	ZINB	0.0000	0.0003	-5.33	Poisson	0.5714	0.9986	-0.17
OTU_16	Ascomycota	Saccharomycetes	Saccharomycetales	Incertae sedis	Debaryomyces	ZINB	0.9742	0.9988	263.58	ZINB	0.0456	0.3362	170.83	ZINB	0.9661	0.9986	263.58
OTU_2	unassigned	unassigned	unassigned	unassigned	unassigned	NB	0.5234	0.9988	492.87	ZINB	0.2988	0.9971	976.42	NB	0.0004	0.0045	1516.00
OTU_20	Ascomycota	Sordariomycetes	Sordariales	Chaetomiaceae	unassigned	ZINB	0.4379	0.9988	72.20	ZINB	0.9632	0.9971	95.50	ZINB	0.0002	0.0031	94.83
OTU_223	Basidiomycota	Wallemiomycetes	Wallemiales	Wallemiaceae	Wallemia	ZINB	0.9906	0.9988	9.08	ZINB	0.9890	0.9971	9.08	ZINB	0.0000	0.0002	8.75
OTU_26	Basidiomycota	Incertae sedis	Malasseziales	Malasseziaceae	Malassezia	ZINB	0.6743	0.9988	30.48	ZINB	0.0000	0.0004	67.58	ZINB	0.9687	0.9986	69.08
OTU_3	Ascomycota	Dothideomycetes	Capnodiales	Davidiellaceae	unassigned	ZINB	0.0022	0.1026	-743.87	ZINB	0.9789	0.9971	1.08	ZINB	0.0422	0.3497	23.67
OTU_34	Ascomycota	Dothideomycetes	Pleosporales	Pleosporaceae	Curvularia	ZINB	0.9920	0.9988	3.25	ZINB	0.0000	0.0000	-34.00	ZINB	0.9931	0.9986	3.25
OTU_36	Basidiomycota	Microbotryomycetes	Sporidiobolales	Incertae sedis	Rhodotorula	ZINB	0.9783	0.9988	16.92	ZINB	0.0063	0.0533	15.42	ZINB	0.0061	0.0594	14.92
OTU_4	Ascomycota	Saccharomycetes	Saccharomycetales	Incertae sedis	Candida	ZINB	0.0070	0.1636	852.63	ZINB	0.5987	0.9971	432.83	ZINB	0.0000	0.0002	915.50
OTU_52	Basidiomycota	Tremellomycetes	Cystofilobasidiales	Cystofilobasidiaceae	Cystofilobasidium	ZINB	0.0000	0.0000	-38.47	ZINB	0.9921	0.9971	2.83	ZINB	0.9932	0.9986	2.83
OTU_62	Ascomycota	Dothideomycetes	Dothideales	Dothioraceae	Aureobasidium	ZINB	0.9893	0.9988	18.08	ZINB	0.0000	0.0000	17.58	ZINB	0.9879	0.9986	18.08
OTU_9	Ascomycota	Dothideomycetes	Pleosporales	Pleosporaceae	Alternaria	ZINB	0.0057	0.1636	-1.57	ZINB	0.9971	0.9971	0.33	ZINB	0.9975	0.9986	0.33

Table S7. Significantly differential KEGG pathways between UC-MCS. Table sorted by Kruskal-Wallis p-value (p-value<0.05, q-value <0.0006). Linear mixed-effects regression models were applied to determine pairwise differences amongst UC-MCS (p-value<0.05).

Super-Pathway	Sub-Pathway	Pathway	MCS1-2_Model	MCS1-2_pvalue	MCS1-2_change	MCS1-3_Model	MCS1-3_pvalue	MCS1-3_change	MCS1-4_Model	MCS1-4_pvalue	MCS1-4_change
Cellular Processes	Transport and Catabolism	Lysosome	NB	0.0000	24783.72	NB	0.0000	33276.17	NB	0.0000	46344.92
Metabolism	Glycan Biosynthesis and Metabolism	Other glycan degradation	NB	0.0000	47202.57	NB	0.0000	80069.92	NB	0.0000	112469.67
Metabolism	Lipid Metabolism	Sphingolipid metabolism	NB	0.0000	28504.83	NB	0.0000	52168.33	NB	0.0000	70893.17
Metabolism	Glycan Biosynthesis and Metabolism	Glycosaminoglycan degradation	NB	0.0000	20153.77	NB	0.0000	23016.67	NB	0.0000	31103.00
Metabolism	Lipid Metabolism	Steroid hormone biosynthesis	NB	0.0000	6262.67	NB	0.0564	6093.92	NB	0.0000	8210.83
Metabolism	Glycan Biosynthesis and Metabolism	Glycosphingolipid biosynthesis - globo series	NB	0.0001	12350.78	NB	0.0000	19128.33	NB	0.0000	29750.92

Metabolism	Glycan Biosynthesis and Metabolism	Glycosphingolipid biosynthesis - ganglio series	NB	0.0000	15207.68	NB	0.0017	13817.58	NB	0.0000	23438.75
Metabolism	Biosynthesis of Other Secondary Metabolites	Penicillin and cephalosporin biosynthesis	NB	0.0001	3279.52	NB	0.0000	6683.17	NB	0.0000	5241.75
Human Diseases	Infectious Diseases	Pertussis	NB	0.0000	5208.70	NB	0.0000	6540.75	NB	0.1564	-10803.67
Metabolism	Metabolism of Cofactors and Vitamins	Ubiquinone and other terpenoid-quinone biosynthesis	NB	0.0014	10491.20	NB	0.0001	-18773.50	NB	0.0249	-21918.50
Unclassified	Genetic Information Processing	Restriction enzyme	NB	0.5647	2347.48	NB	0.0000	23709.58	NB	0.0000	37134.42
Genetic Information Processing	Folding, Sorting and Degradation	Ubiquitin system	NB	0.0063	1689.57	NB	0.0000	4088.42	NB	0.2654	-1298.67
Environmental Information Processing	Signaling Molecules and Interaction	Cellular antigens	NB	0.0000	6453.45	NB	0.2250	-2538.25	NB	0.3202	2232.25
Organismal Systems	Digestive System	Protein digestion and absorption	NB	0.0000	5369.62	NB	0.6429	-779.08	NB	0.0043	4745.42
Organismal Systems	Endocrine System	PPAR signaling pathway	NB	0.5062	-1446.47	NB	0.0000	10704.08	NB	0.0000	9816.50
Human Diseases	Metabolic Diseases	Type II diabetes mellitus	NB	0.0000	-5177.30	NB	0.9130	-177.25	NB	0.4077	1105.17
Metabolism	Metabolism of Terpenoids and Polyketides	Biosynthesis of siderophore group nonribosomal peptides	NB	0.0033	1470.35	NB	0.1101	-1612.75	NB	0.0014	-8530.08
Organismal Systems	Digestive System	Carbohydrate digestion and absorption	NB	0.0005	-3544.23	NB	0.0000	-6366.08	NB	0.0048	-3752.00
Organismal Systems	Excretory System	Proximal tubule bicarbonate reclamation	NB	0.4239	798.42	NB	0.0000	4782.42	NB	0.0000	5310.75
Unclassified	Metabolism	Nucleotide metabolism	NB	0.0026	-3989.03	NB	0.3311	1740.92	NB	0.0002	-14963.00
Metabolism	Biosynthesis of Other Secondary Metabolites	Butirosin and neomycin biosynthesis	NB	0.0014	-7090.93	NB	0.0527	4494.42	NB	0.0000	10312.17
Metabolism	Biosynthesis of Other Secondary Metabolites	Streptomycin biosynthesis	NB	0.3473	-7221.42	NB	0.0006	25543.33	NB	0.0000	41253.25
Metabolism	Xenobiotics Biodegradation and Metabolism	Metabolism of xenobiotics by cytochrome P450	NB	0.0033	-3713.83	NB	0.0285	2906.67	NB	0.0003	-12039.83
Metabolism	Metabolism of Other Amino Acids	Phosphonate and phosphinate metabolism	NB	0.1127	-2514.82	NB	0.0000	10502.83	NB	0.0167	3381.25
Metabolism	Carbohydrate Metabolism	Galactose metabolism	NB	0.5136	-13856.33	NB	0.0004	103665.92	NB	0.0000	101600.33
Human Diseases	Infectious Diseases	African trypanosomiasis	NB	0.1759	-605.08	NB	0.0144	719.17	NB	0.0008	-4712.42
Metabolism	Xenobiotics Biodegradation and Metabolism	Drug metabolism - cytochrome P450	NB	0.0029	-3797.80	NB	0.0408	2773.50	NB	0.0003	-12027.17
Genetic Information Processing	Translation	Ribosome biogenesis in eukaryotes	NB	0.0001	-4278.27	NB	0.8378	334.08	NB	0.2618	-1819.67
Metabolism	Lipid Metabolism	Arachidonic acid metabolism	NB	0.9040	88.92	NB	0.0000	-13067.58	NB	0.0018	-4284.75
Metabolism	Xenobiotics Biodegradation and Metabolism	Bisphenol degradation	NB	0.5727	-1448.17	NB	0.0029	12265.58	NB	0.0000	17891.00
Metabolism	Lipid Metabolism	Secondary bile acid biosynthesis	NB	0.9644	71.45	NB	0.0002	9238.75	NB	0.0000	7341.75
Metabolism	Lipid Metabolism	Primary bile acid biosynthesis	NB	0.9459	109.02	NB	0.0002	9287.42	NB	0.0000	7355.92
Metabolism	Lipid Metabolism	Linoleic acid metabolism	NB	0.9394	-175.35	NB	0.0021	11639.50	NB	0.0000	17459.75
Human Diseases	Infectious Diseases	Bacterial invasion of epithelial cells	NB	0.0014	-366.92	NB	0.0014	94.08	NB	0.0001	-653.92
Environmental Information Processing	Signaling Molecules and Interaction	Ion channels	NB	0.1473	-1118.68	NB	0.4529	969.17	NB	0.0001	-9173.42
Environmental Information Processing	Signaling Molecules and Interaction	Bacterial toxins	NB	0.0598	-6252.22	NB	0.0056	13277.08	NB	0.0187	7645.58
Human Diseases	Infectious Diseases	Chagas disease (American trypanosomiasis)	NB	0.3122	-542.78	NB	0.0455	713.92	NB	0.0113	-4729.42
Metabolism	Metabolism of Cofactors and Vitamins	Lipoic acid metabolism	NB	0.0386	2195.08	NB	0.0000	7279.33	NB	0.9689	91.25
Metabolism	Lipid Metabolism	Fatty acid metabolism	NB	0.0010	-16012.43	NB	0.0114	17567.67	NB	0.0932	-18959.33
Metabolism	Biosynthesis of Other Secondary Metabolites	beta-Lactam resistance	NB	0.4724	1011.10	NB	0.0064	6388.25	NB	0.0000	8819.17
Human Diseases	Cancers	Bladder cancer	NB	0.1323	-97.02	NB	0.2868	28.58	NB	0.0027	-1340.92
Metabolism	Biosynthesis of Other Secondary Metabolites	Tropane, piperidine and pyridine alkaloid biosynthesis	NB	0.0646	-4256.35	NB	0.1766	4271.25	NB	0.0000	11450.25
Metabolism	Energy Metabolism	Methane metabolism	NB	0.0497	-85130.37	NB	0.1710	83186.58	NB	0.0000	172989.00
Human Diseases	Infectious Diseases	Epithelial cell signaling in Helicobacter pylori infection	NB	0.0304	-6127.08	NB	0.9822	-77.08	NB	0.0000	12457.75
Human Diseases	Cancers	Renal cell carcinoma	NB	0.0078	-597.83	NB	0.0494	-524.08	NB	0.0001	-2561.33
Organismal Systems	Nervous System	Glutamatergic synapse	NB	0.8144	-813.48	NB	0.0071	11042.67	NB	0.0000	21892.58

Organismal Systems	Endocrine System	Insulin signaling pathway	NB	0.0080	-7883.17	NB	0.1527	5281.58	NB	0.0000	12510.33
Organismal Systems	Digestive System	Mineral absorption	NB	0.0044	-658.18	NB	0.0000	-4415.08	NB	0.0000	-1815.42
Metabolism	Xenobiotics Biodegradation and Metabolism	Chloroalkane and chloroalkene degradation	NB	0.0047	-18039.37	NB	0.0829	17940.33	NB	0.5257	4723.00
Human Diseases	Infectious Diseases	Staphylococcus aureus infection	NB	0.0015	-2012.83	NB	0.9880	7.92	NB	0.0000	-10241.33
Metabolism	Glycan Biosynthesis and Metabolism	Glycosphingolipid biosynthesis - lacto and neolacto series	ZINB	0.3208	92.43	ZINB	0.0000	227.58	ZINB	0.0000	242.67
Metabolism	Xenobiotics Biodegradation and Metabolism	Naphthalene degradation	NB	0.0013	-13100.77	NB	0.3809	3670.33	NB	0.0338	-10496.67
Metabolism	Xenobiotics Biodegradation and Metabolism	Dioxin degradation	NB	0.0004	-8751.07	NB	0.1494	5242.58	NB	0.0509	-6723.83
Unclassified	Cellular Processes and Signaling	Pores ion channels	NB	0.0000	32535.73	NB	0.0001	25183.83	NB	0.0588	31562.17
Cellular Processes	Cell Growth and Death	Apoptosis	NB	0.0061	-507.77	NB	0.0037	185.83	NB	0.0025	-853.33
Metabolism	Xenobiotics Biodegradation and Metabolism	Xylene degradation	NB	0.0008	-8851.30	NB	0.2075	4719.75	NB	0.3806	-2906.50
Metabolism	Carbohydrate Metabolism	C5-Branched dibasic acid metabolism	NB	0.0071	-25434.82	NB	0.1172	25000.33	NB	0.0503	21974.42
Metabolism	Amino Acid Metabolism	Arginine and proline metabolism	NB	0.1331	-53826.23	NB	0.0782	100881.67	NB	0.0000	169931.83
Environmental Information Processing	Signal Transduction	Phosphatidylinositol signaling system	NB	0.3314	-1700.30	NB	0.0001	9130.00	NB	0.1078	2981.33
Organismal Systems	Immune System	RIG-I-like receptor signaling pathway	NB	0.0723	-531.65	NB	0.0075	574.75	NB	0.0077	-1662.42
Environmental Information Processing	Membrane Transport	Phosphotransferase system (PTS)	NB	0.0103	-44544.07	NB	0.1584	30115.33	NB	0.0005	-112435.50
Metabolism	Amino Acid Metabolism	Histidine metabolism	NB	0.2296	-21077.92	NB	0.0540	56878.83	NB	0.0000	94038.92
Metabolism	Metabolism of Terpenoids and Polyketides	Polyketide sugar unit biosynthesis	NB	0.8827	-799.62	NB	0.0086	15182.08	NB	0.0000	36538.75
Metabolism	Metabolism of Terpenoids and Polyketides	Tetracycline biosynthesis	NB	0.0533	-12993.85	NB	0.0735	15573.00	NB	0.0000	25966.08
Metabolism	Glycan Biosynthesis and Metabolism	Lipopolysaccharide biosynthesis	NB	0.0010	21775.72	NB	0.0188	-20152.33	NB	0.5499	7710.25
Metabolism	Metabolism of Cofactors and Vitamins	Biotin metabolism	NB	0.7215	-1258.88	NB	0.0119	12997.42	NB	0.0000	26540.42
Unclassified	Cellular Processes and Signaling	Other transporters	NB	0.1561	-10070.52	NB	0.0405	18914.83	NB	0.0000	33735.75
Metabolism	Carbohydrate Metabolism	Pyruvate metabolism	NB	0.0410	-63390.87	NB	0.0587	83404.83	NB	0.0009	105365.50
Genetic Information Processing	Folding, Sorting and Degradation	Proteasome	NB	0.0052	-2761.93	NB	0.6122	736.92	NB	0.1527	1810.17
Genetic Information Processing	Folding, Sorting and Degradation	Protein export	NB	0.0215	-32909.55	NB	0.6086	10287.25	NB	0.0030	46643.58
Unclassified	Cellular Processes and Signaling	Membrane and intracellular structural molecules	NB	0.0000	38223.68	NB	0.2489	12242.58	NB	0.0050	54711.58
Metabolism	Metabolism of Terpenoids and Polyketides	Biosynthesis of vancomycin group antibiotics	NB	0.9072	166.00	NB	0.0130	2914.00	NB	0.0000	6959.17
Metabolism	Biosynthesis of Other Secondary Metabolites	Isoquinoline alkaloid biosynthesis	NB	0.0918	1623.38	NB	0.5471	-890.67	NB	0.0000	6576.75
Metabolism	Amino Acid Metabolism	Valine, leucine and isoleucine biosynthesis	NB	0.0156	-57409.80	NB	0.1188	61259.25	NB	0.0158	64626.33
Metabolism	Carbohydrate Metabolism	Fructose and mannose metabolism	NB	0.2808	-34589.58	NB	0.0415	76693.92	NB	0.0000	137018.42
Unclassified	Cellular Processes and Signaling	Sporulation	NB	0.0241	-100770.45	NB	0.7123	23433.75	NB	0.0180	185021.58
Organismal Systems	Endocrine System	Adipocytokine signaling pathway	NB	0.4747	1032.07	NB	0.0000	6051.42	NB	0.0636	3103.17
Metabolism	Amino Acid Metabolism	Lysine biosynthesis	NB	0.0344	-56080.18	NB	0.2345	46339.67	NB	0.0012	89019.25
Metabolism	Metabolism of Terpenoids and Polyketides	Geraniol degradation	NB	0.0001	3650.18	NB	0.0655	2027.08	NB	0.1480	-6750.75
Genetic Information Processing	Transcription	RNA polymerase	NB	0.0011	-14250.63	NB	0.9839	129.17	NB	0.6436	2600.67
Metabolism	Metabolism of Terpenoids and Polyketides	Zeatin biosynthesis	NB	0.4389	-795.03	NB	0.0835	-2045.58	NB	0.0000	5485.83
Human Diseases	Cancers	Pathways in cancer	NB	0.1004	-1972.40	NB	0.3938	-1229.50	NB	0.0000	6192.83
Human Diseases	Infectious Diseases	Tuberculosis	NB	0.0195	-8968.03	NB	0.6440	2386.67	NB	0.0027	12465.67
Metabolism	Xenobiotics Biodegradation and Metabolism	Chlorocyclohexane and chlorobenzene degradation	NB	0.2529	-650.30	NB	0.0030	1772.25	NB	0.0049	-3240.50
Metabolism	Carbohydrate Metabolism	Glyoxylate and dicarboxylate metabolism	NB	0.2284	-17266.58	NB	0.0262	49669.42	NB	0.0000	72758.92

Metabolism	Metabolism of Terpenoids and Polyketides	Limonene and pinene degradation	NB	0.0029	-6974.70	NB	0.6579	-1088.25	NB	0.0024	-12346.33
Metabolism	Xenobiotics Biodegradation and Metabolism	Drug metabolism - other enzymes	NB	0.0658	-12420.73	NB	0.5913	4249.17	NB	0.0000	29819.33
Metabolism	Biosynthesis of Other Secondary Metabolites	Novobiocin biosynthesis	NB	0.0645	-5845.25	NB	0.1884	6576.00	NB	0.0007	12008.58
Genetic Information Processing	Transcription	Transcription machinery	NB	0.4049	-21176.38	NB	0.1430	49233.42	NB	0.0000	182020.08
Human Diseases	Metabolic Diseases	Type I diabetes mellitus	NB	0.2623	-1340.45	NB	0.0170	3499.50	NB	0.0002	4116.75
Metabolism	Amino Acid Metabolism	Alanine, aspartate and glutamate metabolism	NB	0.3831	-24964.18	NB	0.0808	72535.67	NB	0.0000	136519.08
Metabolism	Lipid Metabolism	Fatty acid biosynthesis	NB	0.1050	-24053.63	NB	0.2122	24275.42	NB	0.0000	58680.67
Metabolism	Nucleotide Metabolism	Pyrimidine metabolism	NB	0.0208	-102307.30	NB	0.9958	319.25	NB	0.0274	109067.67
Metabolism	Energy Metabolism	Carbon fixation pathways in prokaryotes	NB	0.2478	-26353.57	NB	0.3953	23965.58	NB	0.0000	107366.67
Cellular Processes	Cell Motility	Cytoskeleton proteins	NB	0.0392	-28690.92	NB	0.5052	12409.33	NB	0.0000	65768.42
Metabolism	Energy Metabolism	Carbon fixation in photosynthetic organisms	NB	0.1373	-27537.65	NB	0.3412	21937.50	NB	0.0001	71207.08
Unclassified	Metabolism	Amino acid metabolism	NB	0.4168	-4188.10	NB	0.0271	14820.00	NB	0.0000	22700.33
Metabolism	Lipid Metabolism	Glycerolipid metabolism	NB	0.0080	-37532.57	NB	0.2373	23455.58	NB	0.0452	30442.17
Metabolism	Metabolism of Other Amino Acids	D-Glutamine and D-glutamate metabolism	NB	0.1279	-5251.33	NB	0.3214	4653.42	NB	0.0007	12114.33
Metabolism	Metabolism of Cofactors and Vitamins	One carbon pool by folate	NB	0.0958	-23182.38	NB	0.5664	-10359.83	NB	0.0010	50988.75
Metabolism	Carbohydrate Metabolism	Inositol phosphate metabolism	NB	0.5665	-1758.38	NB	0.0000	12881.92	NB	0.1093	5477.08
Metabolism	Biosynthesis of Other Secondary Metabolites	Flavonoid biosynthesis	NB	0.0000	-2134.67	NB	0.1075	-765.92	NB	0.7828	-144.67
Metabolism	Energy Metabolism	Oxidative phosphorylation	NB	0.4735	-20799.53	NB	0.3052	35728.67	NB	0.0000	145896.67
Environmental Information Processing	Signal Transduction	MAPK signaling pathway - yeast	NB	0.3239	1289.93	NB	0.0040	7823.33	NB	0.0008	5930.33
Genetic Information Processing	Translation	Translation factors	NB	0.0156	-31207.78	NB	0.9104	-2001.33	NB	0.0100	37143.75
Genetic Information Processing	Translation	Aminoacyl-tRNA biosynthesis	NB	0.0018	-98271.77	NB	0.9870	713.83	NB	0.2437	43930.33
Genetic Information Processing	Replication and Repair	Nucleotide excision repair	NB	0.0075	-26226.05	NB	0.8428	-2773.25	NB	0.1071	18713.25
Metabolism	Carbohydrate Metabolism	Amino sugar and nucleotide sugar metabolism	NB	0.3461	-31808.58	NB	0.0234	96471.67	NB	0.0000	127306.58
Metabolism	Metabolism of Terpenoids and Polyketides	Biosynthesis of ansamycins	NB	0.1099	-7431.77	NB	0.3428	6204.58	NB	0.0004	17447.17
Metabolism	Xenobiotics Biodegradation and Metabolism	Nitrotoluene degradation	NB	0.1709	-6092.03	NB	0.4811	4922.67	NB	0.0004	16132.33
Metabolism	Glycan Biosynthesis and Metabolism	Lipopolysaccharide biosynthesis proteins	NB	0.0001	29164.52	NB	0.8101	-1980.58	NB	0.4442	12960.08
Metabolism	Amino Acid Metabolism	Phenylalanine, tyrosine and tryptophan biosynthesis	NB	0.0385	-56259.52	NB	0.3873	35667.58	NB	0.0019	91572.75
Genetic Information Processing	Replication and Repair	DNA replication proteins	NB	0.0181	-67827.08	NB	0.9307	3397.92	NB	0.0077	84641.92
Metabolism	Metabolism of Cofactors and Vitamins	Pantothenate and CoA biosynthesis	NB	0.0764	-32399.92	NB	0.2808	28714.58	NB	0.0016	61736.58
Genetic Information Processing	Replication and Repair	Base excision repair	NB	0.0086	-28807.75	NB	0.5266	9643.25	NB	0.0120	28992.25
Unclassified	Cellular Processes and Signaling	Cell division	NB	0.8975	-342.85	NB	0.2337	3962.75	NB	0.0000	14991.42
Metabolism	Metabolism of Terpenoids and Polyketides	Terpenoid backbone biosynthesis	NB	0.0236	-31919.90	NB	0.9050	-2274.25	NB	0.0139	39495.17
Genetic Information Processing	Translation	Ribosome	NB	0.0056	-159431.48	NB	0.7467	-25897.33	NB	0.0867	115890.25
Unclassified	Poorly Characterized	General function prediction only	NB	0.0904	-153523.15	NB	0.3025	130031.50	NB	0.0010	306384.08
Metabolism	Amino Acid Metabolism	Amino acid related enzymes	NB	0.0336	-82218.45	NB	0.5403	33154.50	NB	0.0150	104682.92
Metabolism	Carbohydrate Metabolism	Pentose phosphate pathway	NB	0.0785	-49846.95	NB	0.1043	65732.25	NB	0.0028	86984.42
Metabolism	Lipid Metabolism	Lipid biosynthesis proteins	NB	0.1018	-23845.17	NB	0.2814	22245.08	NB	0.0001	55642.50
Metabolism	Carbohydrate Metabolism	Pentose and glucuronate interconversions	NB	0.9373	-1324.85	NB	0.0124	78337.75	NB	0.0000	97887.42
Metabolism	Carbohydrate Metabolism	Propanoate metabolism	NB	0.0099	-35179.27	NB	0.1522	26878.08	NB	0.1241	24442.67

Organismal Systems	Endocrine System	Progesterone-mediated oocyte maturation	NB	0.2646	-1360.02	NB	0.6128	-705.67	NB	0.0000	8753.92
Organismal Systems	Immune System	Antigen processing and presentation	NB	0.2646	-1360.02	NB	0.6128	-705.67	NB	0.0000	8753.92
Unclassified	Metabolism	Energy metabolism	NB	0.2581	-24805.07	NB	0.3854	22613.33	NB	0.0000	108025.83
Metabolism	Metabolism of Cofactors and Vitamins	Porphyrin and chlorophyll metabolism	NB	0.5544	-22162.45	NB	0.1862	80294.50	NB	0.0000	241017.42
Genetic Information Processing	Replication and Repair	Homologous recombination	NB	0.0181	-55998.20	NB	0.8569	5727.75	NB	0.0479	52831.00
Metabolism	Xenobiotics Biodegradation and Metabolism	Styrene degradation	NB	0.0050	-1929.95	NB	0.0502	1500.00	NB	0.8503	181.08
Genetic Information Processing	Folding, Sorting and Degradation	Protein processing in endoplasmic reticulum	NB	0.5522	805.47	NB	0.4157	1289.67	NB	0.0000	14147.00
Metabolism	Xenobiotics Biodegradation and Metabolism	Benzoate degradation	NB	0.0022	-21146.18	NB	0.3106	9424.42	NB	0.3506	-9038.25
Human Diseases	Cancers	Prostate cancer	NB	0.4799	-872.77	NB	0.8678	239.33	NB	0.0000	9753.17
Genetic Information Processing	Replication and Repair	Mismatch repair	NB	0.0212	-49920.63	NB	0.9710	-1071.58	NB	0.0241	54702.50
Metabolism	Amino Acid Metabolism	Phenylalanine metabolism	NB	0.7812	-1174.67	NB	0.0041	17559.58	NB	0.0000	20976.00
Cellular Processes	Cell Growth and Death	Cell cycle - Caulobacter	NB	0.0585	-26292.75	NB	0.9742	-627.25	NB	0.0033	44253.92
Genetic Information Processing	Translation	RNA transport	NB	0.0546	-11754.87	NB	0.4595	6448.08	NB	0.0018	20108.00
Organismal Systems	Immune System	NOD-like receptor signaling pathway	NB	0.8255	-259.65	NB	0.4118	1151.00	NB	0.0000	10542.75
Genetic Information Processing	Replication and Repair	Chromosome	NB	0.0410	-85886.12	NB	0.9840	-1089.42	NB	0.0054	119236.08
Metabolism	Metabolism of Terpenoids and Polyketides	Carotenoid biosynthesis	NB	0.0000	-1959.92	NB	0.2497	-404.67	NB	0.0087	-1754.08
Genetic Information Processing	Folding, Sorting and Degradation	RNA degradation	NB	0.1609	-13702.75	NB	0.3450	13675.00	NB	0.0001	39289.58
Unclassified	Genetic Information Processing	Translation proteins	NB	0.0061	-65817.00	NB	0.9759	-999.25	NB	0.1204	43112.33
Metabolism	Metabolism of Cofactors and Vitamins	Thiamine metabolism	NB	0.0756	-26024.28	NB	0.3108	23427.42	NB	0.0083	43167.75
Metabolism	Carbohydrate Metabolism	Butanoate metabolism	NB	0.0159	-38859.25	NB	0.0801	40691.75	NB	0.5612	14340.58

Table S8. Significantly differential KEGG pathways between MCS1 and MCS2. Table sorted by Linear mixed-effects regression p-value (p-value<0.05, q-value <0.08).

Super Pathway	Sub Pathway	Pathway	Selected Model	pvalue	qvalue	MCS1-MCS2	Morgan Selected Model	Morgan pvalue	Morgan qvalue	Morgan MCS1-MCS2	Gevers Selected Model	Gevers pvalue	Gevers qvalue	Gevers MCS1-MCS2
Human Diseases	Infectious Diseases	Pertussis	NB	0.0000	0.0000	5208.70	ZINB	0.0012	0.0029	131.75	NB	0.0409	0.0840	309.79
Human Diseases	Cancers	Colorectal cancer	ZINB	0.0000	0.0000	-14.55	NB	0.9977	0.8802	-0.54	NB	0.9981	0.9981	-0.21
Cellular Processes	Cell Growth and Death	p53 signaling pathway	ZINB	0.0000	0.0000	-14.55	NB	0.9977	0.8802	-0.54	NB	0.9981	0.9981	-0.21
Human Diseases	Cancers	Small cell lung cancer	ZINB	0.0000	0.0000	-14.55	NB	0.9977	0.8802	-0.54	NB	0.9981	0.9981	-0.21
Human Diseases	Infectious Diseases	Toxoplasmosis	ZINB	0.0000	0.0000	-14.55	NB	0.9977	0.8802	-0.54	NB	0.9981	0.9981	-0.21
Human Diseases	Cardiovascular Diseases	Viral myocarditis	ZINB	0.0000	0.0000	-14.55	NB	0.9977	0.8802	-0.54	NB	0.9981	0.9981	-0.21
Genetic Information Processing	Transcription	Basal transcription factors	NB	0.0000	0.0000	-390.68	NB	0.1161	0.1442	-2.56	NB	0.3569	0.4851	-1.48
Metabolism	Glycan Biosynthesis and Metabolism	Glycosphingolipid biosynthesis - ganglio series	NB	0.0000	0.0000	15207.68	NB	0.0000	0.0000	574.71	NB	0.0023	0.0111	1255.29
Metabolism	Glycan Biosynthesis and Metabolism	Glycosaminoglycan degradation	NB	0.0000	0.0000	20153.77	NB	0.0000	0.0000	705.67	NB	0.0015	0.0093	1729.48

Environmental Information Processing	Signaling Molecules and Interaction	Cellular antigens	NB	0.0000	0.0000	6453.45	NB	0.0002	0.0008	172.33	NB	0.0011	0.0082	441.30
Cellular Processes	Transport and Catabolism	Lysosome	NB	0.0000	0.0000	24783.72	NB	0.0000	0.0000	742.64	NB	0.0001	0.0042	2043.92
Organismal Systems	Digestive System	Protein digestion and absorption	NB	0.0000	0.0000	5369.62	NB	0.0007	0.0019	139.90	NB	0.0103	0.0320	377.74
Metabolism	Lipid Metabolism	Steroid hormone biosynthesis	NB	0.0000	0.0000	6262.67	NB	0.0000	0.0002	216.07	NB	0.0110	0.0324	401.24
Unclassified	Cellular Processes and Signaling	Membrane and intracellular structural molecules	NB	0.0000	0.0001	38223.68	NB	0.0223	0.0328	813.42	NB	0.0847	0.1535	1834.37
Metabolism	Metabolism of Terpenoids and Polyketides	Carotenoid biosynthesis	NB	0.0000	0.0001	-1959.92	NB	0.0063	0.0110	-22.08	NB	0.8089	0.9426	-14.53
Human Diseases	Metabolic Diseases	Type II diabetes mellitus	NB	0.0000	0.0001	-5177.30	NB	0.0033	0.0065	-109.45	NB	0.0344	0.0743	-273.85
Unclassified	Cellular Processes and Signaling	Pores ion channels	NB	0.0000	0.0002	32535.73	NB	0.0000	0.0001	948.54	NB	0.0371	0.0781	1292.59
Metabolism	Glycan Biosynthesis and Metabolism	Other glycan degradation	NB	0.0000	0.0002	47202.57	NB	0.0012	0.0030	1038.92	NB	0.0218	0.0522	2578.02
Metabolism	Lipid Metabolism	Sphingolipid metabolism	NB	0.0000	0.0003	28504.83	NB	0.1944	0.2287	299.55	NB	0.2160	0.3167	1008.46
Metabolism	Biosynthesis of Other Secondary Metabolites	Flavonoid biosynthesis	NB	0.0000	0.0003	-2134.67	NB	0.0121	0.0198	-31.30	NB	0.3670	0.4963	-52.52
Metabolism	Glycan Biosynthesis and Metabolism	Glycosphingolipid biosynthesis - globo series	NB	0.0001	0.0005	12350.78	NB	0.0001	0.0003	414.54	NB	0.0110	0.0324	896.96
Metabolism	Biosynthesis of Other Secondary Metabolites	Penicillin and cephalosporin biosynthesis	NB	0.0001	0.0005	3279.52	NB	0.0855	0.1123	59.72	NB	0.0205	0.0500	241.35
Human Diseases	Infectious Diseases	Influenza A	NB	0.0001	0.0005	-112.25	NB	0.9977	0.8802	-0.54	NB	0.9968	0.9981	-0.60
Metabolism	Metabolism of Terpenoids and Polyketides	Geraniol degradation	NB	0.0001	0.0006	3650.18	NB	0.0002	0.0008	112.24	NB	0.1461	0.2368	170.26
Metabolism	Glycan Biosynthesis and Metabolism	Lipopolysaccharide biosynthesis proteins	NB	0.0001	0.0006	29164.52	NB	0.0000	0.0002	1138.96	NB	0.0138	0.0367	1945.22
Genetic Information Processing	Translation	Ribosome biogenesis in eukaryotes	NB	0.0001	0.0008	-4278.27	NB	0.0000	0.0000	-142.40	NB	0.0001	0.0042	-355.79
Organismal Systems	Circulatory System	Cardiac muscle contraction	NB	0.0003	0.0018	-44.95	ZINB	0.9946	0.8802	-1.62	ZINB	0.9955	0.9981	-0.70
Metabolism	Xenobiotics Biodegradation and Metabolism	Dioxin degradation	NB	0.0004	0.0024	-8751.07	NB	0.0003	0.0010	-316.16	NB	0.0585	0.1137	-469.10
Organismal Systems	Digestive System	Carbohydrate digestion and absorption	NB	0.0005	0.0035	-3544.23	NB	0.9591	0.8802	1.99	NB	0.4312	0.5694	-93.71
Metabolism	Xenobiotics Biodegradation and Metabolism	Xylene degradation	NB	0.0008	0.0051	-8851.30	NB	0.0002	0.0008	-320.24	NB	0.0321	0.0710	-519.80
Metabolism	Lipid Metabolism	Fatty acid metabolism	NB	0.0010	0.0058	-16012.43	NB	0.0003	0.0010	-594.06	NB	0.0019	0.0106	-1401.61
Metabolism	Glycan Biosynthesis and Metabolism	Lipopolysaccharide biosynthesis	NB	0.0010	0.0060	21775.72	NB	0.0008	0.0021	921.91	NB	0.0257	0.0593	1735.65
Genetic Information Processing	Transcription	RNA polymerase	NB	0.0011	0.0061	-14250.63	NB	0.0002	0.0008	-492.73	NB	0.0011	0.0082	-1178.84
Metabolism	Xenobiotics Biodegradation and Metabolism	Naphthalene degradation	NB	0.0013	0.0072	-13100.77	NB	0.0059	0.0107	-333.83	NB	0.4320	0.5694	-308.49
Metabolism	Biosynthesis of Other Secondary Metabolites	Butirosin and neomycin biosynthesis	NB	0.0014	0.0072	-7090.93	NB	0.0003	0.0009	-207.28	NB	0.0066	0.0232	-621.40
Metabolism	Metabolism of Cofactors and Vitamins	Ubiquinone and other terpenoid-quinone biosynthesis	NB	0.0014	0.0072	10491.20	NB	0.0403	0.0555	243.71	NB	0.1513	0.2417	575.54
Human Diseases	Infectious Diseases	Bacterial invasion of epithelial cells	NB	0.0014	0.0072	-366.92	NB	0.1695	0.2016	-1.24	NB	0.6747	0.8153	4.64
Human Diseases	Infectious Diseases	Staphylococcus aureus infection	NB	0.0015	0.0072	-2012.83	NB	0.0209	0.0313	-53.10	NB	0.1967	0.2967	90.50
Genetic Information Processing	Replication and Repair	Non-homologous end-joining	NB	0.0016	0.0075	-2599.80	NB	0.1112	0.1392	-34.75	NB	0.8408	0.9710	23.73
Organismal Systems	Digestive System	Bile secretion	NB	0.0016	0.0075	-97.37	NB	0.2576	0.2784	0.55	NB	0.9980	0.9981	-0.40
Genetic Information Processing	Translation	Aminoacyl-tRNA biosynthesis	NB	0.0018	0.0083	-98271.77	NB	0.0000	0.0001	-3776.88	NB	0.0001	0.0042	-9076.89
Metabolism	Xenobiotics Biodegradation and Metabolism	Benzoate degradation	NB	0.0022	0.0098	-21146.18	NB	0.0000	0.0000	-747.06	NB	0.0001	0.0042	-1641.21
Unclassified	Genetic Information Processing	Replication, recombination and repair proteins	NB	0.0022	0.0098	-65148.12	NB	0.0000	0.0000	-2918.21	NB	0.0026	0.0121	-5420.10
Unclassified	Metabolism	Nucleotide metabolism	NB	0.0026	0.0113	-3989.03	NB	0.0000	0.0001	-149.41	NB	0.0004	0.0057	-537.77
Human Diseases	Neurodegenerative Diseases	Parkinson's disease	NB	0.0028	0.0114	-71.28	ZINB	0.9916	0.8802	-2.15	NB	0.3228	0.4457	-2.77
Metabolism	Xenobiotics Biodegradation and Metabolism	Drug metabolism - cytochrome P450	NB	0.0029	0.0114	-3797.80	NB	0.0346	0.0489	-67.93	NB	0.5805	0.7214	-71.69
Metabolism	Metabolism of Terpenoids and Polyketides	Limonene and pinene degradation	NB	0.0029	0.0114	-6974.70	NB	0.0152	0.0244	-142.30	NB	0.0786	0.1445	-475.44
Environmental Information Processing	Membrane Transport	Secretion system	NB	0.0031	0.0122	-82733.18	NB	0.0000	0.0000	-3442.35	NB	0.0000	0.0042	-7831.60
Metabolism	Lipid Metabolism	Biosynthesis of unsaturated fatty acids	NB	0.0032	0.0122	-8229.32	NB	0.0001	0.0005	-318.13	NB	0.0020	0.0107	-684.70

Metabolism	Xenobiotics Biodegradation and Metabolism	Metabolism of xenobiotics by cytochrome P450	NB	0.0033	0.0122	-3713.83	NB	0.0397	0.0551	-65.56	NB	0.5630	0.7031	-73.63
Metabolism	Metabolism of Terpenoids and Polyketides	Biosynthesis of siderophore group nonribosomal peptides	NB	0.0033	0.0122	1470.35	NB	0.1181	0.1458	32.46	NB	0.0984	0.1723	117.13
Human Diseases	Infectious Diseases	Vibrio cholerae infection	NB	0.0039	0.0139	-97.20	Poisson	0.9976	0.8802	0.20	NB	0.9968	0.9981	-0.72
Organismal Systems	Digestive System	Mineral absorption	NB	0.0044	0.0153	-658.18	NB	0.0375	0.0526	-15.41	NB	0.8903	0.9981	-4.07
Metabolism	Lipid Metabolism	Steroid biosynthesis	ZINB	0.0044	0.0153	-132.12	ZINB	0.0103	0.0174	-1.49	NB	0.8981	0.9981	4.57
Metabolism	Xenobiotics Biodegradation and Metabolism	Chloroalkane and chloroalkene degradation	NB	0.0047	0.0157	-18039.37	NB	0.0019	0.0042	-765.21	NB	0.0328	0.0719	-1281.90
Organismal Systems	Environmental Adaptation	Circadian rhythm - plant	NB	0.0047	0.0157	-14.43	NB	0.9977	0.8802	-0.59	ZINB	0.9943	0.9981	1.56
Metabolism	Amino Acid Metabolism	Tryptophan metabolism	NB	0.0049	0.0161	-7697.43	NB	0.0033	0.0065	-269.80	NB	0.0083	0.0273	-766.18
Metabolism	Xenobiotics Biodegradation and Metabolism	Styrene degradation	NB	0.0050	0.0162	-1929.95	NB	0.0603	0.0812	-56.43	NB	0.7293	0.8738	-35.43
Metabolism	Metabolism of Other Amino Acids	D-Alanine metabolism	NB	0.0051	0.0163	-7831.58	NB	0.0000	0.0000	-363.33	NB	0.0002	0.0042	-683.26
Genetic Information Processing	Folding, Sorting and Degradation	Proteasome	NB	0.0052	0.0164	-2761.93	NB	0.0001	0.0005	-116.63	NB	0.1814	0.2769	-140.83
Metabolism	Amino Acid Metabolism	Tyrosine metabolism	NB	0.0056	0.0168	-22198.52	NB	0.0002	0.0008	-863.66	NB	0.0145	0.0379	-1522.95
Genetic Information Processing	Translation	Ribosome	NB	0.0056	0.0168	-159431.48	NB	0.0000	0.0003	-6521.02	NB	0.0007	0.0075	-14989.06
Cellular Processes	Cell Growth and Death	Apoptosis	NB	0.0061	0.0179	-507.77	NB	0.2077	0.2406	4.93	NB	0.2150	0.3167	13.70
Unclassified	Genetic Information Processing	Translation proteins	NB	0.0061	0.0179	-65817.00	NB	0.0000	0.0001	-2706.61	NB	0.0002	0.0042	-6322.14
Genetic Information Processing	Folding, Sorting and Degradation	Ubiquitin system	NB	0.0063	0.0182	1689.57	NB	0.0002	0.0008	50.98	NB	0.1003	0.1734	77.90
Metabolism	Carbohydrate Metabolism	C5-Branched dibasic acid metabolism	NB	0.0071	0.0200	-25434.82	NB	0.0045	0.0087	-892.74	NB	0.0120	0.0335	-2274.61
Genetic Information Processing	Replication and Repair	Nucleotide excision repair	NB	0.0075	0.0210	-26226.05	NB	0.0000	0.0002	-1197.70	NB	0.0063	0.0231	-2250.71
Human Diseases	Neurodegenerative Diseases	Alzheimer's disease	NB	0.0077	0.0210	-3143.12	NB	0.0000	0.0001	-137.30	NB	0.0002	0.0042	-323.10
Human Diseases	Cancers	Renal cell carcinoma	NB	0.0078	0.0210	-597.83	NB	0.6656	0.6504	4.50	NB	0.4722	0.6132	-24.73
Organismal Systems	Endocrine System	Insulin signaling pathway	NB	0.0080	0.0210	-7883.17	NB	0.0025	0.0052	-264.39	NB	0.1086	0.1840	-456.24
Metabolism	Lipid Metabolism	Glycerolipid metabolism	NB	0.0080	0.0210	-37532.57	NB	0.0001	0.0004	-1609.94	NB	0.0016	0.0096	-4253.72
Human Diseases	Immune System Diseases	Systemic lupus erythematosus	NB	0.0082	0.0210	-14.17	ZINB	0.9970	0.8802	-0.56	ZINB	0.9943	0.9981	1.56
Environmental Information Processing	Membrane Transport	Bacterial secretion system	NB	0.0082	0.0210	-35381.05	NB	0.0000	0.0002	-1448.71	NB	0.0123	0.0337	-2560.69
Genetic Information Processing	Replication and Repair	Base excision repair	NB	0.0086	0.0218	-28807.75	NB	0.0018	0.0041	-1089.37	NB	0.0068	0.0233	-2592.39
Metabolism	Carbohydrate Metabolism	Glycolysis / Gluconeogenesis	NB	0.0087	0.0218	-81591.93	NB	0.0001	0.0005	-3362.62	NB	0.0012	0.0082	-8822.46
Metabolism	Carbohydrate Metabolism	Propanoate metabolism	NB	0.0099	0.0243	-35179.27	NB	0.0003	0.0010	-1313.94	NB	0.0009	0.0081	-4226.26
Unclassified	Cellular Processes and Signaling	Electron transfer carriers	NB	0.0101	0.0246	-2607.75	NB	0.0677	0.0906	-73.12	NB	0.4791	0.6191	142.97
Environmental Information Processing	Membrane Transport	Phosphotransferase system (PTS)	NB	0.0103	0.0248	-44544.07	NB	0.0078	0.0136	-2222.34	NB	0.0065	0.0232	-9680.11
Metabolism	Metabolism of Cofactors and Vitamins	Nicotinate and nicotinamide metabolism	NB	0.0107	0.0253	-26443.45	NB	0.0002	0.0008	-1166.79	NB	0.0006	0.0068	-2863.94
Genetic Information Processing	Transcription	Transcription factors	NB	0.0121	0.0282	-146377.65	NB	0.0000	0.0001	-7039.49	NB	0.0011	0.0082	-16065.59
Metabolism	Glycan Biosynthesis and Metabolism	Peptidoglycan biosynthesis	NB	0.0128	0.0295	-56861.32	NB	0.0001	0.0006	-2388.32	NB	0.0020	0.0107	-5311.84
Genetic Information Processing	Replication and Repair	DNA replication	NB	0.0129	0.0295	-37640.65	NB	0.0003	0.0011	-1572.05	NB	0.0072	0.0243	-3588.09
Metabolism	Biosynthesis of Other Secondary Metabolites	Caffeine metabolism	NB	0.0134	0.0303	-14.33	ZINB	0.9970	0.8802	-0.56	NB	0.8938	0.9981	1.81
Genetic Information Processing	Translation	Ribosome Biogenesis	NB	0.0138	0.0307	-95429.97	NB	0.0000	0.0003	-4163.92	NB	0.0002	0.0042	-10299.39
Genetic Information Processing	Replication and Repair	DNA repair and recombination proteins	NB	0.0145	0.0320	-174099.60	NB	0.0003	0.0010	-7353.02	NB	0.0024	0.0115	-17348.98
Metabolism	Amino Acid Metabolism	Valine, leucine and isoleucine biosynthesis	NB	0.0156	0.0332	-57409.80	NB	0.0004	0.0013	-2387.05	NB	0.0040	0.0165	-5507.60
Genetic Information Processing	Translation	Translation factors	NB	0.0156	0.0332	-31207.78	NB	0.0002	0.0008	-1335.64	NB	0.0025	0.0118	-3029.13
Metabolism	Xenobiotics Biodegradation and Metabolism	Toluene degradation	NB	0.0157	0.0332	4408.80	NB	0.2434	0.2669	120.70	NB	0.4538	0.5923	271.85

Metabolism	Carbohydrate Metabolism	Butanoate metabolism	NB	0.0159	0.0332	-38859.25	NB	0.0000	0.0001	-1787.59	NB	0.0011	0.0082	-4630.64
Metabolism	Amino Acid Metabolism	Cysteine and methionine metabolism	NB	0.0160	0.0332	-55138.93	NB	0.0001	0.0003	-2612.63	NB	0.0015	0.0093	-6365.28
Metabolism	Xenobiotics Biodegradation and Metabolism	Aminobenzoate degradation	NB	0.0170	0.0351	-6202.88	NB	0.4586	0.4643	-49.72	NB	0.5409	0.6798	-163.32
Metabolism	Xenobiotics Biodegradation and Metabolism	Ethylbenzene degradation	NB	0.0172	0.0351	-3625.62	NB	0.2739	0.2932	-37.17	NB	0.7705	0.9100	42.46
Genetic Information Processing	Replication and Repair	DNA replication proteins	NB	0.0181	0.0361	-67827.08	NB	0.0002	0.0008	-3037.18	NB	0.0088	0.0283	-6609.41
Genetic Information Processing	Replication and Repair	Homologous recombination	NB	0.0181	0.0361	-55998.20	NB	0.0002	0.0008	-2341.86	NB	0.0011	0.0082	-5858.03
Environmental Information Processing	Membrane Transport	Transporters	NB	0.0195	0.0379	-577669.37	NB	0.0001	0.0003	-27416.73	NB	0.0012	0.0082	-60831.18
Human Diseases	Infectious Diseases	Tuberculosis	NB	0.0195	0.0379	-8968.03	NB	0.0000	0.0001	-421.81	NB	0.0005	0.0063	-1052.18
Unclassified	Cellular Processes and Signaling	Signal transduction mechanisms	NB	0.0196	0.0379	-37826.33	NB	0.0000	0.0002	-1709.60	NB	0.0003	0.0042	-4237.07
Metabolism	Nucleotide Metabolism	Pyrimidine metabolism	NB	0.0208	0.0397	-102307.30	NB	0.0002	0.0008	-4592.93	NB	0.0016	0.0096	-11270.98
Genetic Information Processing	Replication and Repair	Mismatch repair	NB	0.0212	0.0402	-49920.63	NB	0.0001	0.0007	-2242.91	NB	0.0021	0.0107	-5451.15
Genetic Information Processing	Folding, Sorting and Degradation	Protein export	NB	0.0215	0.0402	-32909.55	NB	0.0007	0.0019	-1418.83	NB	0.0067	0.0233	-3088.95
Metabolism	Carbohydrate Metabolism	Ascorbate and aldarate metabolism	NB	0.0217	0.0402	-8230.27	NB	0.1111	0.1392	-223.53	NB	0.0360	0.0764	-1410.04
Metabolism	Metabolism of Terpenoids and Polyketides	Terpenoid backbone biosynthesis	NB	0.0236	0.0434	-31919.90	NB	0.0001	0.0003	-1553.43	NB	0.0005	0.0060	-3787.37
Unclassified	Cellular Processes and Signaling	Sporulation	NB	0.0241	0.0439	-100770.45	NB	0.0000	0.0000	-4983.05	NB	0.0000	0.0042	-12428.44
Environmental Information Processing	Membrane Transport	ABC transporters	NB	0.0260	0.0469	-261825.17	NB	0.0000	0.0003	-13597.33	NB	0.0034	0.0146	-26514.30
Metabolism	Nucleotide Metabolism	Purine metabolism	NB	0.0275	0.0491	-112073.68	NB	0.0021	0.0045	-5135.12	NB	0.0081	0.0270	-11752.80
Human Diseases	Infectious Diseases	Epithelial cell signaling in Helicobacter pylori infection	NB	0.0304	0.0538	-6127.08	NB	0.0025	0.0052	-280.22	NB	0.0170	0.0439	-613.10
Metabolism	Metabolism of Cofactors and Vitamins	Vitamin B6 metabolism	NB	0.0320	0.0560	-8857.17	NB	0.0005	0.0014	-386.61	NB	0.0202	0.0498	-878.51
Metabolism	Amino Acid Metabolism	Amino acid related enzymes	NB	0.0336	0.0582	-82218.45	NB	0.0002	0.0008	-3991.51	NB	0.0010	0.0082	-9392.80
Metabolism	Amino Acid Metabolism	Lysine biosynthesis	NB	0.0344	0.0592	-56080.18	NB	0.0007	0.0020	-2684.03	NB	0.0106	0.0323	-5521.23
Human Diseases	Infectious Diseases	Pathogenic Escherichia coli infection	ZINB	0.0349	0.0595	-55.00	ZINB	0.9971	0.8802	-0.38	NB	0.9963	0.9981	-11.28
Metabolism	Metabolism of Other Amino Acids	Selenocompound metabolism	NB	0.0368	0.0621	-18972.77	NB	0.0005	0.0013	-1018.27	NB	0.0030	0.0136	-2181.59
Metabolism	Amino Acid Metabolism	Phenylalanine, tyrosine and tryptophan biosynthesis	NB	0.0385	0.0631	-56259.52	NB	0.0009	0.0024	-2559.61	NB	0.0031	0.0137	-6344.96
Metabolism	Lipid Metabolism	Fatty acid elongation in mitochondria	NB	0.0385	0.0631	-14.23	ZINB	0.9970	0.8802	-0.56	ZINB	0.9943	0.9981	1.56
Metabolism	Metabolism of Cofactors and Vitamins	Lipoic acid metabolism	NB	0.0386	0.0631	2195.08	NB	0.0000	0.0002	143.04	NB	0.0008	0.0079	402.07
Metabolism	Lipid Metabolism	Synthesis and degradation of ketone bodies	NB	0.0387	0.0631	-2505.27	NB	0.0000	0.0001	-134.71	NB	0.0021	0.0107	-253.99
Cellular Processes	Cell Motility	Cytoskeleton proteins	NB	0.0392	0.0634	-28690.92	NB	0.0000	0.0001	-1488.47	NB	0.0004	0.0057	-3461.48
Unclassified	Genetic Information Processing	Protein folding and associated processing	NB	0.0396	0.0634	-24596.90	NB	0.0391	0.0546	-1068.89	NB	0.2748	0.3898	-1495.34
Genetic Information Processing	Replication and Repair	Chromosome	NB	0.0410	0.0645	-85886.12	NB	0.0001	0.0005	-4263.85	NB	0.0009	0.0079	-10500.59
Metabolism	Carbohydrate Metabolism	Pyruvate metabolism	NB	0.0410	0.0645	-63390.87	NB	0.0014	0.0033	-2773.01	NB	0.0110	0.0324	-6384.55
Unclassified	Metabolism	Lipid metabolism	NB	0.0477	0.0744	-9976.45	NB	0.0019	0.0042	-444.75	NB	0.0121	0.0335	-918.24
Metabolism	Energy Metabolism	Methane metabolism	NB	0.0497	0.0770	-85130.37	NB	0.0020	0.0044	-3960.12	NB	0.0095	0.0302	-9258.12

Table S9. Mantel Test results comparing distance matrices generated from 16S rRNA composition, *in silico* predicted bacterial metagenome, and metabolomic data

Distance Matrix 1	Distance Matrix 2	Number of samples	Correlation Method	Mantel r statistic	p-value	Number of permutations	Tail type
Metabolome (Canberra Distance)	16S rRNA - MiSeq (Weighted UniFrac Distance)	43	Spearman	0.3802	0.0001	10000	two sided
Metabolome (Canberra Distance)	Bacterial Metagenome (Bray Curtis Distance)	43	Spearman	0.2100	0.008	10000	two sided

Table S10. Significantly differential fecal metabolites between MCS-1 and MCS-2. Table sorted by fold change in abundance. Welch's T-test p-value<0.05.

SUPER PATHWAY	SUB PATHWAY	BIOCHEMICAL	pvalue	q_value	Fold Change (MCS1 / MCS2_
Lipid	Long Chain Fatty Acid	myristate (14:0)	0.020368741	0.839698313	0.253474093
Xenobiotics	Food Component/Plant	phytanate	0.02013954	0.839698313	0.282456371
Xenobiotics	Food Component/Plant	indolin-2-one	0.045770501	0.839698313	0.314504449
Amino Acid	Phenylalanine and Tyrosine Metabolism	o-Tyrosine	0.049904293	0.839698313	0.320531572
Lipid	Fatty Acid, Branched	isopalmitic acid	0.018573267	0.839698313	0.421310454
Peptide	Gamma-glutamyl Amino Acid	gamma-glutamylglutamine	0.042657368	0.839698313	0.499699152
Lipid	Sterol	lathosterol	0.0116081	0.839698313	0.520027958
Amino Acid	Tryptophan Metabolism	N-acetyltryptophan	0.021974958	0.839698313	1.608321118
Lipid	Lysolipid	2-palmitoylglycerophosphocholine*	0.021605381	0.839698313	1.724163459
Lipid	Fatty Acid, Monohydroxy	2-hydroxyoctanoate	0.008849528	0.839698313	2.021205569
Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	N-acetylmethionine sulfoxide	0.034365624	0.839698313	2.058056075
Amino Acid	Glutamate Metabolism	gamma-aminobutyrate (GABA)	0.029219323	0.839698313	2.337160488
Xenobiotics	Food Component/Plant	vanillate	0.022548124	0.839698313	2.607916966
Nucleotide	Pyrimidine Metabolism, Uracil containing	uridine-2',3'-cyclic monophosphate	0.03444455	0.839698313	2.637515575
Peptide	Gamma-glutamyl Amino Acid	gamma-glutamylalanine	0.029782874	0.839698313	3.112231026
Amino Acid	Alanine and Aspartate Metabolism	N-propionylalanine	0.009288137	0.839698313	3.23524498
Xenobiotics	Food Component/Plant	2-oxindole-3-acetate	0.040421329	0.839698313	3.547056618
Lipid	Fatty Acid, Dihydroxy	9,10-DiHOME	0.007672813	0.839698313	3.585314389
Lipid	Lysolipid	1-stearoylglycerophosphoserine*	0.033844727	0.839698313	3.75720175
Xenobiotics	Food Component/Plant	2,3-dihydroxyisovalerate	0.010454061	0.839698313	3.883700219
Xenobiotics	Food Component/Plant	glycitein	0.039587409	0.839698313	4.012180511
Amino Acid	Polyamine Metabolism	agmatine	0.045994016	0.839698313	4.021215111
Nucleotide	Purine Metabolism, Adenine containing	adenosine 5'-monophosphate (AMP)	0.044954124	0.839698313	4.190413451
Amino Acid	Tryptophan Metabolism	indolelactate	0.004669039	0.839698313	4.362958019

Carbohydrate	Pentose Metabolism	threitol	0.021852787	0.839698313	4.964977831
Lipid	Fatty Acid, Monohydroxy	13-HODE + 9-HODE	0.00569308	0.839698313	4.965176606
Lipid	Lysolipid	1-linoleoylglycerophosphocholine (18:2n6)	0.027510832	0.839698313	5.883665272
Amino Acid	Histidine Metabolism	histamine	0.049651623	0.839698313	5.994803748
Lipid	Lysolipid	1-stearoylglycerophosphocholine (18:0)	0.004687218	0.839698313	7.472804973
Amino Acid	Polyamine Metabolism	putrescine	0.019873276	0.839698313	10.46100576
Lipid	Fatty Acid Metabolism(Acyl Carnitine)	palmitoylcarnitine	0.016917767	0.839698313	11.010959

Table S11. Significantly differential fecal metabolites between MCS-1 and MCS-3. Table sorted by fold change in abundance. Welch's T-test p-value<0.05.

SUPER PATHWAY	SUB PATHWAY	BIOCHEMICAL	pvalue	q_value	Fold Change (MCS1 / MCS3)
Lipid	Lysolipid	1-linoleoylglycerophosphoethanolamine*	0.042803627	0.34745598	64.58531746
Cofactors and Vitamins	Nicotinate and Nicotinamide Metabolism	N1-Methyl-2-pyridone-5-carboxamide	0.006098163	0.253145171	23.11976048
Lipid	Steroid	4-androsten-3alpha,17alpha-diol monosulfate (2)	0.025874171	0.344205776	23.06659948
Amino Acid	Phenylalanine and Tyrosine Metabolism	3-(3-hydroxyphenyl)propionate	0.011768157	0.263269364	14.74779419
Lipid	Neurotransmitter	acetylcholine	0.01873906	0.326721631	14.58153094
Amino Acid	Glutathione Metabolism	ophthalmate	0.041682114	0.344986519	12.40974152
Lipid	Secondary Bile Acid Metabolism	tauroursodeoxycholate	0.021160898	0.330013632	11.25306212
Amino Acid	Phenylalanine and Tyrosine Metabolism	3-(4-hydroxyphenyl)propionate	0.046901557	0.354288267	10.68476036
Lipid	Steroid	4-androsten-3beta,17beta-diol disulfate (2)	0.025209418	0.344205776	10.24797118
Amino Acid	Urea cycle; Arginine and Proline Metabolism	N-acetylproline	0.033056412	0.344986519	9.240209572
Lipid	Carnitine Metabolism	deoxycarnitine	0.007196616	0.253145171	9.100596201
Amino Acid	Phenylalanine and Tyrosine Metabolism	p-cresol sulfate	0.026094295	0.344205776	9.004219205
Nucleotide	Pyrimidine Metabolism, Thymine containing	3-aminoisobutyrate	0.007012029	0.253145171	8.995617992
Lipid	Secondary Bile Acid Metabolism	ursodeoxycholate	0.039291188	0.344986519	8.795978025
Lipid	Polyunsaturated Fatty Acid (n3 and n6)	mead acid (20:3n9)	0.011850355	0.263269364	8.277816086
Lipid	Steroid	pregnenolone sulfate	0.046637535	0.354288267	7.631324525
Xenobiotics	Xanthine Metabolism	1-methylurate	0.040390704	0.344986519	7.598940598
Lipid	Polyunsaturated Fatty Acid (n3 and n6)	docosadienoate (22:2n6)	0.045358785	0.354288267	6.671487603
Xenobiotics	Food Component/Plant	2,3-dihydroxyisovalerate	0.00426964	0.253145171	5.609333773
Amino Acid	Urea cycle; Arginine and Proline Metabolism	homocitrulline	0.003176742	0.253145171	5.101749751
Lipid	Endocannabinoid	palmitoyl ethanolamide	0.03638649	0.344986519	4.39223995
Lipid	Secondary Bile Acid Metabolism	hyocholate	0.031453365	0.344986519	4.105870671
Xenobiotics	Benzoate Metabolism	4-hydroxybenzoate	0.009185964	0.258497319	4.091544353

Lipid	Secondary Bile Acid Metabolism	3b-hydroxy-5-cholenoic acid	0.0218910880.330013632	3.498261266
Lipid	Endocannabinoid	stearoyl ethanolamide	0.0172589530.316744567	3.385964912
Lipid	Steroid	5alpha-pregnan-3beta,20beta-diol monosulfate (1)	0.0115238930.263269364	2.538744329
Xenobiotics	Benzoate Metabolism	3-hydroxybenzoate	0.0087560070.258497319	2.465168484
Amino Acid	Polyamine Metabolism	acisoga	0.0313357670.344986519	2.049640232
Amino Acid	Alanine and Aspartate Metabolism	asparagine	0.0470026380.354288267	0.70518651
Amino Acid	Glycine, Serine and Threonine Metabolism	serine	0.0323790380.344986519	0.667045466
Peptide	Dipeptide	alanylisoleucine	0.0137065860.289282301	0.624870176
Amino Acid	Lysine Metabolism	lysine	0.0111246360.263269364	0.619363646
Amino Acid	Histidine Metabolism	trans-urocanate	0.040948960.344986519	0.618522773
Peptide	Dipeptide	leucylalanine	0.006873330.253145171	0.602927373
Peptide	Dipeptide	phenylalanylaspartate	0.0231932740.337587708	0.513090523
Amino Acid	Histidine Metabolism	cis-urocanate	0.0333382730.344986519	0.506069029
Peptide	Dipeptide	alanylglutamine	0.0046118650.253145171	0.504820614
Peptide	Dipeptide	glycylvaline	0.0053469060.253145171	0.503759622
Lipid	Inositol Metabolism	myo-inositol	0.0331041150.344986519	0.472450928
Peptide	Dipeptide	arginylvaline	0.0347709130.344986519	0.442668701
Peptide	Dipeptide	glycylproline	0.0070443880.253145171	0.439461153
Peptide	Dipeptide	glycylisoleucine	0.0168580910.316744567	0.438640065
Nucleotide	Purine Metabolism, Guanine containing	2'-O-methylguanosine	0.0209566120.330013632	0.434860116
Peptide	Dipeptide	serylisoleucine	0.0390227740.344986519	0.430000667
Peptide	Dipeptide	glycylthreonine	0.0012539610.176435242	0.427192911
Peptide	Dipeptide	phenylalanylglycine	0.019350640.326721631	0.420061176
Peptide	Dipeptide	glycylglycine	0.0002052790.086649705	0.414257216
Peptide	Dipeptide	serylvaline	0.0405440940.344986519	0.407521437
Peptide	Dipeptide	cyclo(leu-pro)	0.0005526940.116648006	0.398890315
Peptide	Gamma-glutamyl Amino Acid	gamma-glutamylphenylalanine	0.0377376950.344986519	0.387169258
Peptide	Gamma-glutamyl Amino Acid	gamma-glutamyltyrosine	0.008277550.258497319	0.383101174
Lipid	Medium Chain Fatty Acid	caprate (10:0)	0.0279893010.344986519	0.34747878
Peptide	Dipeptide	asparagylvaline	0.0369039150.344986519	0.331281579
Peptide	Dipeptide	isoleucylphenylalanine	0.0352450250.344986519	0.309052285
Lipid	Phospholipid Metabolism	ethanolamine	0.0289102240.344986519	0.290503634
Peptide	Dipeptide	threonylarginine	0.0158621460.316744567	0.197531861

Table S12. Significantly differential fecal metabolites between MCS-1 and MCS-4. Table sorted by fold change in abundance. Welch's T-test p-value<0.05.

SUPER PATHWAY	SUB PATHWAY	BIOCHEMICAL	pvalue	q_value	Fold Change (MCS1 / MCS4)
Xenobiotics	Drug	4-acetamidophenol	0.016111254	0.060177162	687.0831663
Cofactors and Vitamins	Thiamine Metabolism	thiamin (Vitamin B1)	0.015347088	0.060129671	177.5362705
Lipid	Fatty Acid, Branched	isocaproate	0.014377025	0.059321558	62.97572429
Peptide	Dipeptide Derivative	anserine	0.038988245	0.098802413	60.27347115
Nucleotide	Pyrimidine Metabolism, Orotate containing	N-carbamoylaspartate	0.03035004	0.085880182	41.64462636
Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	3-methylthiopropionate	0.000575932	0.008627769	34.91690613
Amino Acid	Phenylalanine and Tyrosine Metabolism	2-(4-hydroxyphenyl)propionate	0.044970926	0.105810309	32.92188786
Lipid	Steroid	5alpha-androstan-3beta,17beta-diol monosulfate (1)	0.014635185	0.059321558	27.41768648
Amino Acid	Leucine, Isoleucine and Valine Metabolism	isovalerate	6.22E-05	0.002183787	27.02633154
Lipid	Steroid	5alpha-pregnan-3beta,20alpha-diol monosulfate (1)	0.011618541	0.05479413	23.59868729
Xenobiotics	Food Component/Plant	enterolactone	0.045523927	0.105810309	21.79407821
Amino Acid	Urea cycle; Arginine and Proline Metabolism	N-methyl proline	0.014515542	0.059321558	19.46768516
Xenobiotics	Food Component/Plant	3-hydroxycinnamate (m-coumarate)	0.029012861	0.083018857	17.8144702
Nucleotide	Purine Metabolism, (Hypo)Xanthine/Inosine containing	xanthosine	0.043555768	0.104644404	15.44555064
Amino Acid	Phenylalanine and Tyrosine Metabolism	phenylacetate	0.000370978	0.00674833	15.41758047
Lipid	Long Chain Fatty Acid	cis-vaccenate (18:1n7)	0.000178304	0.003784043	12.67770903
Lipid	Fatty Acid, Branched	13-methylmyristic acid	1.43E-05	0.000910442	11.79924623
Peptide	Dipeptide	isoleucyltyrosine	0.03360858	0.091053891	11.65492554
Lipid	Steroid	4-androsten-3beta,17beta-diol monosulfate (2)	0.02469397	0.077639387	11.27969511
Xenobiotics	Food Component/Plant	2-oxindole-3-acetate	0.003817561	0.026139361	10.13132843
Amino Acid	Leucine, Isoleucine and Valine Metabolism	allo-isoleucine	0.006929248	0.037761441	9.981011184
Cofactors and Vitamins	Biotin Metabolism	biotin	0.000976466	0.012251862	9.549763033
Lipid	Polyunsaturated Fatty Acid (n3 and n6)	mead acid (20:3n9)	0.009698456	0.047498015	9.004250327
Amino Acid	Histidine Metabolism	trans-urocanate	0.000213496	0.004182371	8.991121124
Cofactors and Vitamins	Tocopherol Metabolism	delta-tocopherol	0.001726413	0.016611214	8.912547529
Cofactors and Vitamins	Nicotinate and Nicotinamide Metabolism	nicotinamide adenine dinucleotide (NAD+)	0.023774967	0.075684359	8.864595139
Lipid	Long Chain Fatty Acid	palmitoleate (16:1n7)	0.012830514	0.056460255	8.530655506
Lipid	Long Chain Fatty Acid	oleate (18:1n9)	0.001010288	0.012251862	8.446412144
Lipid	Fatty Acid, Monohydroxy	3-hydroxypalmitate	0.005103674	0.031701168	8.314891617
Nucleotide	Purine Metabolism, (Hypo)Xanthine/Inosine containing	inosine	0.006196544	0.035865184	8.092741935
Xenobiotics	Benzoate Metabolism	p-hydroxybenzaldehyde	0.006054763	0.035859555	8.088888889
Peptide	Dipeptide	leucylvaline	0.016135347	0.060177162	7.79268594
Lipid	Steroid	pregnenolone sulfate	0.046836701	0.105810309	7.612516074

Amino Acid	Phenylalanine and Tyrosine Metabolism	N-acetyltyrosine	1.81E-05	0.000921902	7.527777778
Xenobiotics	Food Component/Plant	oleanolate	0.011500581	0.05479413	7.004104271
Amino Acid	Urea cycle; Arginine and Proline Metabolism	ornithine	0.009273948	0.046933742	6.869943651
Energy	TCA Cycle	malate	0.000547881	0.008627769	6.842312157
Nucleotide	Purine Metabolism, Guanine containing	2'-O-methylguanosine	0.002074642	0.017219917	6.240078294
Amino Acid	Histidine Metabolism	formiminoglutamate	0.009398946	0.046933742	6.112026295
Lipid	Polyunsaturated Fatty Acid (n3 and n6)	docosatrienoate (22:3n3)	0.043156318	0.104644404	6.013356779
Nucleotide	Pyrimidine Metabolism, Uracil containing	beta-alanine	0.049193143	0.105810309	5.908498677
Lipid	Fatty Acid, Dicarboxylate	3-carboxy-4-methyl-5-propyl-2-furanpropanoate (CMPF)	0.028263469	0.082733693	5.808720368
Amino Acid	Lysine Metabolism	pipecolate	9.80E-05	0.00226887	5.51526833
Xenobiotics	Food Component/Plant	2-piperidinone	0.046142907	0.105810309	5.335124957
Xenobiotics	Food Component/Plant	4-hydroxybenzyl alcohol	0.036029011	0.095208719	5.15009601
Amino Acid	Lysine Metabolism	glutarate (pentanedioate)	0.015268271	0.060129671	4.980479298
Cofactors and Vitamins	Pterin Metabolism	pterin	0.019505667	0.067622484	4.969901117
Amino Acid	Lysine Metabolism	lysine	0.001943142	0.017219917	4.661752762
Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	methionine sulfoxide	0.006968996	0.037761441	4.501777588
Lipid	Long Chain Fatty Acid	pentadecanoate (15:0)	0.001004749	0.012251862	4.24389839
Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	N-acetylmethionine	0.012048267	0.05567768	4.207448861
Nucleotide	Pyrimidine Metabolism, Thymine containing	thymine	0.002050296	0.017219917	4.014402376
Nucleotide	Purine Metabolism, (Hypo)Xanthine/Inosine containing	xanthine	0.000735379	0.010404349	3.987841838
Lipid	Long Chain Fatty Acid	nervonate (24:1n9)	0.04876585	0.105810309	3.870030088
Xenobiotics	Food Component/Plant	phytol	0.003292731	0.024663433	3.777777778
Amino Acid	Phenylalanine and Tyrosine Metabolism	N-methylphenylalanine	0.036263712	0.095208719	3.631294738
Cofactors and Vitamins	Tocopherol Metabolism	alpha-tocopherol	0.001457188	0.01546253	3.568625227
Cofactors and Vitamins	Pantothenate and CoA Metabolism	pantothenate	0.001430606	0.01546253	3.548406593
Xenobiotics	Food Component/Plant	indolin-2-one	0.041049285	0.101494982	3.433536056
Cofactors and Vitamins	Tocopherol Metabolism	gamma-tocopherol	0.005863196	0.035551778	3.432221763
Amino Acid	Glutamate Metabolism	glutamate	0.001609797	0.01639862	3.367636386
Amino Acid	Alanine and Aspartate Metabolism	N-propionylalanine	0.048695781	0.105810309	2.957446316
Amino Acid	Glutamate Metabolism	glutamine	0.032533443	0.090317391	2.947650324
Amino Acid	Phenylalanine and Tyrosine Metabolism	N-acetylphenylalanine	0.049442309	0.105810309	2.932774799
Xenobiotics	Chemical	3-aminobutyrate	0.04570208	0.105810309	2.704789834
Lipid	Fatty Acid, Dicarboxylate	undecanedioate	0.000548067	0.008627769	2.699968939
Nucleotide	Pyrimidine Metabolism, Uracil containing	uracil	0.038239526	0.098639663	2.694151173
Lipid	Sterol	lanosterol	0.019609523	0.067622484	2.554873918
Amino Acid	Glycine, Serine and Threonine Metabolism	serine	0.003900339	0.026139361	2.516206663
Lipid	Fatty Acid, Branched	isopalmitic acid	0.046127176	0.105810309	2.482235185
Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	methionine	0.039572321	0.098802413	2.361668783
Lipid	Medium Chain Fatty Acid	caproate (6:0)	0.016540687	0.060177162	2.330559473
Amino Acid	Phenylalanine and Tyrosine Metabolism	2-phenylacetamide	0.020567903	0.068921167	2.109756098

Lipid	Fatty Acid, Dicarboxylate	hexadecanedioate	0.022924586	0.074341296	2.009911841
Lipid	Long Chain Fatty Acid	stearate (18:0)	0.016489673	0.060177162	0.644771666
Xenobiotics	Benzoate Metabolism	3,4-dihydroxybenzoate	0.014674959	0.059321558	0.643089312
Amino Acid	Tryptophan Metabolism	tryptophan betaine	0.020348803	0.068921167	0.582382084
Lipid	Long Chain Fatty Acid	arachidate (20:0)	0.049261279	0.105810309	0.581882133
Peptide	Gamma-glutamyl Amino Acid	gamma-glutamylthreonine*	0.033432677	0.091053891	0.535313755
Xenobiotics	Food Component/Plant	syringic acid	0.027291019	0.081988986	0.511827753
Lipid	Steroid	5alpha-pregnan-3beta,20beta-diol monosulfate (1)	0.007152729	0.037949559	0.454354854
Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	cysteine	0.014043137	0.059321558	0.373027533
Xenobiotics	Xanthine Metabolism	7-methylxanthine	0.027495386	0.081988986	0.342110811
Lipid	Secondary Bile Acid Metabolism	3-dehydrocholate	0.022976721	0.074341296	0.331587916
Amino Acid	Urea cycle; Arginine and Proline Metabolism	dimethylarginine (SDMA + ADMA)	9.28E-05	0.00226887	0.328467289
Xenobiotics	Food Component/Plant	maltol	0.028711107	0.083018857	0.318043308
Lipid	Lysolipid	1-stearoylglycerophosphoinositol	0.012243144	0.05567768	0.30904236
Lipid	Lysolipid	1-palmitoylglycerophosphoinositol*	0.041963369	0.102757424	0.286066235
Xenobiotics	Food Component/Plant	vanillate	6.86E-05	0.002183787	0.283263743
Lipid	Secondary Bile Acid Metabolism	12-dehydrocholate	0.002659893	0.021168515	0.263560051
Xenobiotics	Food Component/Plant	nicotianamine	0.004883387	0.03109119	0.244811518
Cofactors and Vitamins	Ascorbate and Aldarate Metabolism	arabonate	0.039402634	0.098802413	0.243537071
Amino Acid	Urea cycle; Arginine and Proline Metabolism	trans-4-hydroxyproline	0.023061153	0.074341296	0.22222698
Peptide	Dipeptide	pyroglutamylglutamine	0.032627441	0.090317391	0.185323475
Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	2-hydroxybutyrate (AHB)	0.026644573	0.081988986	0.182639202
Xenobiotics	Food Component/Plant	naringenin	0.019544381	0.067622484	0.181611277
Xenobiotics	Food Component/Plant	apigenin	0.027623381	0.081988986	0.175828906
Xenobiotics	Food Component/Plant	luteolin	8.85E-05	0.00226887	0.161597356
Amino Acid	Glycine, Serine and Threonine Metabolism	betaine	1.15E-05	0.000910442	0.159385235
Cofactors and Vitamins	Hemoglobin and Porphyrin Metabolism	biliverdin	0.002096122	0.017219917	0.157803295
Nucleotide	Pyrimidine Metabolism, Thymine containing	5,6-dihydrothymine	0.003437014	0.025008604	0.155217224
Cofactors and Vitamins	Hemoglobin and Porphyrin Metabolism	bilirubin (Z,Z)	0.003867492	0.026139361	0.152926638
Xenobiotics	Food Component/Plant	vitexin	0.036026788	0.095208719	0.097323383
Lipid	Carnitine Metabolism	carnitine	0.001268618	0.014685353	0.091051121
Lipid	Inositol Metabolism	myo-inositol	3.77E-06	0.000480051	0.069968526
Lipid	Secondary Bile Acid Metabolism	glycocholenate sulfate*	0.006513908	0.036864242	0.064826413
Xenobiotics	Food Component/Plant	chrysoeriol	3.99E-05	0.001693549	0.063330731
Lipid	Primary Bile Acid Metabolism	chenodeoxycholate	0.00176112	0.016611214	0.062072058
Xenobiotics	Food Component/Plant	2,8-quinolinediol	0.004343968	0.028366007	0.058445916
Lipid	Neurotransmitter	acetylcholine	0.012858628	0.056460255	0.051912295
Lipid	Primary Bile Acid Metabolism	cholate	0.007826423	0.040676487	0.042785809
Lipid	Steroid	5alpha-pregnan-3(alpha or beta),20beta-diol disulfate	0.049392736	0.105810309	0.036833905
Amino Acid	Glutamate Metabolism	pyroglutamine*	0.003094213	0.023878798	0.036304619

Amino Acid	Methionine, Cysteine, SAM and Taurine Metabolism	S-methylcysteine	0.0477887450.105810309	0.034177809
Amino Acid	Glycine, Serine and Threonine Metabolism	O-acetylhomoserine	0.019649280.067622484	0.033291192
Amino Acid	Creatine Metabolism	creatinine	0.0383451620.098639663	0.024845408
Xenobiotics	Benzoate Metabolism	4-hydroxyhippurate	0.0276871190.081988986	0.013323869
Amino Acid	Creatine Metabolism	creatine	2.52E-060.000480051	0.007760627
Lipid	Fatty Acid Metabolism(Acyl Carnitine)	decanoylcarnitine	0.0499225050.105947649	0.005838136
Amino Acid	Leucine, Isoleucine and Valine Metabolism	isobutyrylcarnitine	0.0165346370.060177162	0.003393309

Table S13. Primers used for PCR amplification of the 16S rRNA gene.

SampleID	Golay Barcode Sequence	Linker Sequence	Reverse Primer	Forward Primer
1	TGGTCAACGATA	GTGTGCCAGCMGCCGCGGTAA	GGACTACHVGGGTWTCTAAT	GTGTGCCAGCMGCCGCGGTAA
2	TCCCTTGTCTCC	GTGTGCCAGCMGCCGCGGTAA	GGACTACHVGGGTWTCTAAT	GTGTGCCAGCMGCCGCGGTAA
3	GTAGATCGTGTA	GTGTGCCAGCMGCCGCGGTAA	GGACTACHVGGGTWTCTAAT	GTGTGCCAGCMGCCGCGGTAA
4	TGCATACACTGG	GTGTGCCAGCMGCCGCGGTAA	GGACTACHVGGGTWTCTAAT	GTGTGCCAGCMGCCGCGGTAA
5	GCGATATATCGC	GTGTGCCAGCMGCCGCGGTAA	GGACTACHVGGGTWTCTAAT	GTGTGCCAGCMGCCGCGGTAA
6	CGAGGGAAAGTC	GTGTGCCAGCMGCCGCGGTAA	GGACTACHVGGGTWTCTAAT	GTGTGCCAGCMGCCGCGGTAA
9	CACTACGCTAGA	GTGTGCCAGCMGCCGCGGTAA	GGACTACHVGGGTWTCTAAT	GTGTGCCAGCMGCCGCGGTAA
10	TACTACGTGGCC	GTGTGCCAGCMGCCGCGGTAA	GGACTACHVGGGTWTCTAAT	GTGTGCCAGCMGCCGCGGTAA
11	CGGTCAATTGAC	GTGTGCCAGCMGCCGCGGTAA	GGACTACHVGGGTWTCTAAT	GTGTGCCAGCMGCCGCGGTAA
13	GGTGACTAGTTC	GTGTGCCAGCMGCCGCGGTAA	GGACTACHVGGGTWTCTAAT	GTGTGCCAGCMGCCGCGGTAA
14	CGTAAGATGCCT	GTGTGCCAGCMGCCGCGGTAA	GGACTACHVGGGTWTCTAAT	GTGTGCCAGCMGCCGCGGTAA
15	ACGAGACTGATT	GTGTGCCAGCMGCCGCGGTAA	GGACTACHVGGGTWTCTAAT	GTGTGCCAGCMGCCGCGGTAA
16	AGTCGAACGAGG	GTGTGCCAGCMGCCGCGGTAA	GGACTACHVGGGTWTCTAAT	GTGTGCCAGCMGCCGCGGTAA
17	CGAGCAATCCTA	GTGTGCCAGCMGCCGCGGTAA	GGACTACHVGGGTWTCTAAT	GTGTGCCAGCMGCCGCGGTAA
22	TGCAGTCCTCGA	GTGTGCCAGCMGCCGCGGTAA	GGACTACHVGGGTWTCTAAT	GTGTGCCAGCMGCCGCGGTAA
24	GGCCAGTTCCTA	GTGTGCCAGCMGCCGCGGTAA	GGACTACHVGGGTWTCTAAT	GTGTGCCAGCMGCCGCGGTAA
25	GTGGAGTCTCAT	GTGTGCCAGCMGCCGCGGTAA	GGACTACHVGGGTWTCTAAT	GTGTGCCAGCMGCCGCGGTAA
26	ATGGGTTCCGTC	GTGTGCCAGCMGCCGCGGTAA	GGACTACHVGGGTWTCTAAT	GTGTGCCAGCMGCCGCGGTAA
27	GCGTTCTAGCTG	GTGTGCCAGCMGCCGCGGTAA	GGACTACHVGGGTWTCTAAT	GTGTGCCAGCMGCCGCGGTAA
28	GCTGTACGGATT	GTGTGCCAGCMGCCGCGGTAA	GGACTACHVGGGTWTCTAAT	GTGTGCCAGCMGCCGCGGTAA
29	ACCAGTGACTCA	GTGTGCCAGCMGCCGCGGTAA	GGACTACHVGGGTWTCTAAT	GTGTGCCAGCMGCCGCGGTAA
31	AGTCGTGCACAT	GTGTGCCAGCMGCCGCGGTAA	GGACTACHVGGGTWTCTAAT	GTGTGCCAGCMGCCGCGGTAA
32	ACCATAGCTCCG	GTGTGCCAGCMGCCGCGGTAA	GGACTACHVGGGTWTCTAAT	GTGTGCCAGCMGCCGCGGTAA
33	GATGTTCGCTAG	GTGTGCCAGCMGCCGCGGTAA	GGACTACHVGGGTWTCTAAT	GTGTGCCAGCMGCCGCGGTAA
34	GCTCGAAGATTC	GTGTGCCAGCMGCCGCGGTAA	GGACTACHVGGGTWTCTAAT	GTGTGCCAGCMGCCGCGGTAA

37	TAGGCATGCTTG	GTGTGCCAGCMGCCGCGGTAA	GGACTACHVGGGTWTCTAAT	GTGTGCCAGCMGCCGCGGTAA
38	GTTGTTCTGGGA	GTGTGCCAGCMGCCGCGGTAA	GGACTACHVGGGTWTCTAAT	GTGTGCCAGCMGCCGCGGTAA
40	ATCACCAGGTGT	GTGTGCCAGCMGCCGCGGTAA	GGACTACHVGGGTWTCTAAT	GTGTGCCAGCMGCCGCGGTAA
41	GAATACCAAGTC	GTGTGCCAGCMGCCGCGGTAA	GGACTACHVGGGTWTCTAAT	GTGTGCCAGCMGCCGCGGTAA
43	GTATCTGCGCGT	GTGTGCCAGCMGCCGCGGTAA	GGACTACHVGGGTWTCTAAT	GTGTGCCAGCMGCCGCGGTAA
44	TCGACATCTCTT	GTGTGCCAGCMGCCGCGGTAA	GGACTACHVGGGTWTCTAAT	GTGTGCCAGCMGCCGCGGTAA
46	CTATCTCCTGTC	GTGTGCCAGCMGCCGCGGTAA	GGACTACHVGGGTWTCTAAT	GTGTGCCAGCMGCCGCGGTAA
49	AGGCTTACGTGT	GTGTGCCAGCMGCCGCGGTAA	GGACTACHVGGGTWTCTAAT	GTGTGCCAGCMGCCGCGGTAA
50	AACTAGTTCAGG	GTGTGCCAGCMGCCGCGGTAA	GGACTACHVGGGTWTCTAAT	GTGTGCCAGCMGCCGCGGTAA
51	GGACTTCCAGCT	GTGTGCCAGCMGCCGCGGTAA	GGACTACHVGGGTWTCTAAT	GTGTGCCAGCMGCCGCGGTAA
54	GAACACTTTGGA	GTGTGCCAGCMGCCGCGGTAA	GGACTACHVGGGTWTCTAAT	GTGTGCCAGCMGCCGCGGTAA
55	ACTCACAGGAAT	GTGTGCCAGCMGCCGCGGTAA	GGACTACHVGGGTWTCTAAT	GTGTGCCAGCMGCCGCGGTAA
58	TAACGTGTGTGC	GTGTGCCAGCMGCCGCGGTAA	GGACTACHVGGGTWTCTAAT	GTGTGCCAGCMGCCGCGGTAA
59	TCTCTACCACTC	GTGTGCCAGCMGCCGCGGTAA	GGACTACHVGGGTWTCTAAT	GTGTGCCAGCMGCCGCGGTAA
74	ATTCTGCCGAAG	GTGTGCCAGCMGCCGCGGTAA	GGACTACHVGGGTWTCTAAT	GTGTGCCAGCMGCCGCGGTAA
75	CAAATTCGGGAT	GTGTGCCAGCMGCCGCGGTAA	GGACTACHVGGGTWTCTAAT	GTGTGCCAGCMGCCGCGGTAA
78	CTCACAACCGTG	GTGTGCCAGCMGCCGCGGTAA	GGACTACHVGGGTWTCTAAT	GTGTGCCAGCMGCCGCGGTAA
79	ATCGCACAGTAA	GTGTGCCAGCMGCCGCGGTAA	GGACTACHVGGGTWTCTAAT	GTGTGCCAGCMGCCGCGGTAA

Table S14. Primers used for PCR amplification of the ITS2 region.

SampleID	Golay Barcode Sequence	Linker Sequence	Reverse Primer	Forward Primer
1	GTAATGCGTAAC	GTGTGCCAGCMGCCGCGGTAA	TCCTCCGCTTATTGATATGC	GTGARTCATCGAATCTTTG
2	GTCGAATTTGCG	GTGTGCCAGCMGCCGCGGTAA	TCCTCCGCTTATTGATATGC	GTGARTCATCGAATCTTTG
3	GTCGCCGTACAT	GTGTGCCAGCMGCCGCGGTAA	TCCTCCGCTTATTGATATGC	GTGARTCATCGAATCTTTG
4	GCATCAGAGTTA	GTGTGCCAGCMGCCGCGGTAA	TCCTCCGCTTATTGATATGC	GTGARTCATCGAATCTTTG
5	GTGGTCATCGTA	GTGTGCCAGCMGCCGCGGTAA	TCCTCCGCTTATTGATATGC	GTGARTCATCGAATCTTTG
6	GGAATCCGATTA	GTGTGCCAGCMGCCGCGGTAA	TCCTCCGCTTATTGATATGC	GTGARTCATCGAATCTTTG
9	CTGAAGGGCGAA	GTGTGCCAGCMGCCGCGGTAA	TCCTCCGCTTATTGATATGC	GTGARTCATCGAATCTTTG
10	CGCTCACAGAAT	GTGTGCCAGCMGCCGCGGTAA	TCCTCCGCTTATTGATATGC	GTGARTCATCGAATCTTTG
11	ATTCGGTAGTGC	GTGTGCCAGCMGCCGCGGTAA	TCCTCCGCTTATTGATATGC	GTGARTCATCGAATCTTTG
13	CGAGCTGTTACC	GTGTGCCAGCMGCCGCGGTAA	TCCTCCGCTTATTGATATGC	GTGARTCATCGAATCTTTG
14	CAACACATGCTG	GTGTGCCAGCMGCCGCGGTAA	TCCTCCGCTTATTGATATGC	GTGARTCATCGAATCTTTG
15	ATTCTCTCACGT	GTGTGCCAGCMGCCGCGGTAA	TCCTCCGCTTATTGATATGC	GTGARTCATCGAATCTTTG
16	CGACTCTAAACG	GTGTGCCAGCMGCCGCGGTAA	TCCTCCGCTTATTGATATGC	GTGARTCATCGAATCTTTG
17	GTCTTCAGCAAG	GTGTGCCAGCMGCCGCGGTAA	TCCTCCGCTTATTGATATGC	GTGARTCATCGAATCTTTG

22GAACGGGACGTA	GTGTGCCAGCMGCCGCGGTAA	TCCTCCGCTTATTGATATGC	GTGARTCATCGAATCTTTG
24ACGTGTAGGCTT	GTGTGCCAGCMGCCGCGGTAA	TCCTCCGCTTATTGATATGC	GTGARTCATCGAATCTTTG
25TACGGATTATGG	GTGTGCCAGCMGCCGCGGTAA	TCCTCCGCTTATTGATATGC	GTGARTCATCGAATCTTTG
26GCCTGTCTGCAA	GTGTGCCAGCMGCCGCGGTAA	TCCTCCGCTTATTGATATGC	GTGARTCATCGAATCTTTG
27ATAGCGAACTCA	GTGTGCCAGCMGCCGCGGTAA	TCCTCCGCTTATTGATATGC	GTGARTCATCGAATCTTTG
28TTCGATGCCGCA	GTGTGCCAGCMGCCGCGGTAA	TCCTCCGCTTATTGATATGC	GTGARTCATCGAATCTTTG
29CCAGATATAGCA	GTGTGCCAGCMGCCGCGGTAA	TCCTCCGCTTATTGATATGC	GTGARTCATCGAATCTTTG
31AACTTTCAGGAG	GTGTGCCAGCMGCCGCGGTAA	TCCTCCGCTTATTGATATGC	GTGARTCATCGAATCTTTG
32TAACGCTGTGTG	GTGTGCCAGCMGCCGCGGTAA	TCCTCCGCTTATTGATATGC	GTGARTCATCGAATCTTTG
33AACCAAACTCGA	GTGTGCCAGCMGCCGCGGTAA	TCCTCCGCTTATTGATATGC	GTGARTCATCGAATCTTTG
34GGTCTCCTACAG	GTGTGCCAGCMGCCGCGGTAA	TCCTCCGCTTATTGATATGC	GTGARTCATCGAATCTTTG
37GAGAGTCCACTT	GTGTGCCAGCMGCCGCGGTAA	TCCTCCGCTTATTGATATGC	GTGARTCATCGAATCTTTG
38TTCTCCATCACA	GTGTGCCAGCMGCCGCGGTAA	TCCTCCGCTTATTGATATGC	GTGARTCATCGAATCTTTG
40CTGGGTATCTCG	GTGTGCCAGCMGCCGCGGTAA	TCCTCCGCTTATTGATATGC	GTGARTCATCGAATCTTTG
41GACTACCCGTTG	GTGTGCCAGCMGCCGCGGTAA	TCCTCCGCTTATTGATATGC	GTGARTCATCGAATCTTTG
43ATGGGCGAATGG	GTGTGCCAGCMGCCGCGGTAA	TCCTCCGCTTATTGATATGC	GTGARTCATCGAATCTTTG
44GATCTCTGGGTA	GTGTGCCAGCMGCCGCGGTAA	TCCTCCGCTTATTGATATGC	GTGARTCATCGAATCTTTG
46CATCATACGGGT	GTGTGCCAGCMGCCGCGGTAA	TCCTCCGCTTATTGATATGC	GTGARTCATCGAATCTTTG
49CAACGTGCTCCA	GTGTGCCAGCMGCCGCGGTAA	TCCTCCGCTTATTGATATGC	GTGARTCATCGAATCTTTG
50TACACAAGTCGC	GTGTGCCAGCMGCCGCGGTAA	TCCTCCGCTTATTGATATGC	GTGARTCATCGAATCTTTG
51GCGTCCATGAAT	GTGTGCCAGCMGCCGCGGTAA	TCCTCCGCTTATTGATATGC	GTGARTCATCGAATCTTTG
54CACCCGATGGTT	GTGTGCCAGCMGCCGCGGTAA	TCCTCCGCTTATTGATATGC	GTGARTCATCGAATCTTTG
55AATGACCTCGTG	GTGTGCCAGCMGCCGCGGTAA	TCCTCCGCTTATTGATATGC	GTGARTCATCGAATCTTTG
58GCGTTGCAAACT	GTGTGCCAGCMGCCGCGGTAA	TCCTCCGCTTATTGATATGC	GTGARTCATCGAATCTTTG
59ATCCCTACGGAA	GTGTGCCAGCMGCCGCGGTAA	TCCTCCGCTTATTGATATGC	GTGARTCATCGAATCTTTG
74GGTTCCATTAGG	GTGTGCCAGCMGCCGCGGTAA	TCCTCCGCTTATTGATATGC	GTGARTCATCGAATCTTTG
75TTCCTAGGCCAG	GTGTGCCAGCMGCCGCGGTAA	TCCTCCGCTTATTGATATGC	GTGARTCATCGAATCTTTG
78ACCTTACACCTT	GTGTGCCAGCMGCCGCGGTAA	TCCTCCGCTTATTGATATGC	GTGARTCATCGAATCTTTG
79CCGAGGTATAAT	GTGTGCCAGCMGCCGCGGTAA	TCCTCCGCTTATTGATATGC	GTGARTCATCGAATCTTTG

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CHAPTER 4

Implications and Future Directions

The research described above highlights the importance of the gastrointestinal microbiome in the context of UC, emphasizing its applicability with respect to the identification and development of novel therapeutic mechanisms as well as the improved stratification of this historically heterogeneous patient population. While evidence exists demonstrating the effectiveness of probiotic therapy at maintaining disease remission in UC patients (49), the murine study presented here evidences the ability of microbial supplementation to *induce* remission, supporting preliminary findings by Bibiloni *et al.* and emphasizing the need for larger, well-controlled human trials as well as additional murine experimentation to further elucidate the efficacy and mechanisms behind this effect (6, 14, 49). Interestingly, this work also identified the murine ileal microbiota as the community exhibiting the greatest compositional remodeling during induction and amelioration of UC, a novel observation for this field. Paralleling this study, the multi-facetted characterization of UC patients' gut microbiomes, described in Chapter 3, further illustrates the utility of this microbial assemblage with respect to improved treatment practice and guidelines. In addition to corroborating previous observations regarding a UC-associated depletion of gut bacterial diversity and concomitant significant (though variable) shift in gross bacterial community composition (27-31), this effort provides a comprehensive description of the UC-associated fungal community structure, highlighted by significant *Saccharomycetales* enrichment, and accents the need to incorporate fungal profiling in future UC microbiome studies. Furthermore, this human study establishes the gut microbiome as a novel tool for enhanced patient stratification and identified differential metabolic programming, capable of contributing to disease via modulation of host immune activity, amongst UC patients of differing microbiome composition. Together, these studies illuminate new avenues for the discovery of innovative microbiome-based therapies and patient stratification tools in the context of UC.

The lack of a true cure, variable treatment response rates, frequent need for hospitalization, and desire to avoid colectomy necessitates the development of additional therapeutic strategies for UC (3, 4, 6, 7). The findings described herein suggest that one pathway towards novel therapies lies within the gastrointestinal microbiome. As substantial compositional change in the ileal microbiota accompanied disease onset and amelioration in mice, characterization of the ileal microbiome in UC patients (particularly in the context of high and low disease activity) would further elucidate the contribution of this community to disease. Considering the abundance of immune tissue in the ileum and the ability of the ileal microbiome to regulate intestinal epithelial barrier function (54, 55, 159, 160), substantial opportunity exists within this environment for a dysbiotic community to modulate host immune activity, influencing UC onset and progression, via induction of a leaky epithelial barrier and simultaneous production and translocation of immunomodulatory metabolites. Alternatively, the altered metabolic activity of a dysbiotic ileal microbiota could produce metabolites that reinforce downstream pathogenic communities of colonic microbes through immune modulation or species cross-feeding. This dysbiotic colonic microbiome could then directly drive UC through the production of its own suite of pro-inflammatory metabolites, a concept supported by the *in vitro* work presented in Chapter 3. Though individual immunomodulatory microbial metabolites relevant to UC have been identified (17-21), suggesting microbial metabolism may influence UC, the *in vitro* work presented above advances this concept by characterizing the combined pro-inflammatory influence of the conglomerate metabolome present in the context of UC-dysbiosis. All in all, this work suggests a wealth of therapeutic opportunities exist within the metabolic network of microbes colonizing the lower gastrointestinal tract. With additional investigation into these metabolic pathways and the microbial species that encode them, mechanisms of action, and gastrointestinal sites of influence, these potential opportunities can be translated into transformative therapies for the UC patient population.

The development of innovative therapies for UC, though necessary, will be for naught without the ability to identify those patients most likely to benefit from said treatments. Having a better understanding of characteristic differences amongst UC patients will lead to improved stratification of this population and enhanced application of existing and future treatments (161) (5). The work described in Chapter 3 supports the use of the gastrointestinal microbiota as a distinguishing feature within the UC population. Of note, this study identified a discrete microbial marker (i.e., dominant bacterial family) associated with differing levels of disease activity, an important finding when considering the potential clinical utility of the microbiome as a stratification tool. While this study provides foundational evidence for the existence of distinct microbial states within the UC population that associate with and contribute to differential levels of disease severity, questions pertaining to the development, stability, and resolution of these clinically divergent microbial communities remain. Larger human studies containing additional, finer resolution measures of disease activity could confirm the findings presented here, provide critical information concerning the finite or gradient aspect of such microbial states, and identify the existence of additional unique microbial states of clinical relevance. The inclusion of longitudinal as well as pre- and post-treatment observations in these studies would permit assessment of pathogenic community stability over time or identify key compositional changes in the microbiome that parallel disease progression. Additionally, as noted earlier, parallel profiling of the microbiota present in multiple regions of the lower gastrointestinal tract would improve understanding of the contribution these various microbial communities have in shaping both one another as well as UC. Furthermore, investigation into the immunoregulatory capacity of differential metabolic programs present within the gut of microbially and clinically distinct UC patients, such as those highlighted in Chapter 3, would increase understanding of the mechanistic differences between such patients. Ultimately, studies of this kind could identify additional therapeutic targets while leading to an enhanced ability to predict efficacy of a given therapy in any one UC patient.

Though advances in medicine have significantly reduced the frequency of UC-related deaths (4), the quality of life for UC patients remains substantially lower than that of the general population (162, 163). This stems from the chronic nature of and lack of a true cure for UC. As a result, patients and clinicians are left to a lifetime of symptom management, rather than complete abrogation, using an array of treatment options (3, 6, 7). Despite near continuous treatment and disease monitoring, 50% of patients experience symptom flares at least once a month, 15% experience a severe flare require hospitalization at least once during their lifetime, and approximately 33% receive surgery (7, 164). This suggests significant improvement in both treatment options and practices are needed to significantly improve patient outcomes and reduce the overall burden (medically and financially) of UC. The gastrointestinal microbiome represents a novel arena containing a trove of potential solutions to these issues. This thesis sheds additional light on the importance of gastrointestinal microbial communities in UC and suggests advancements in patient stratification, leading to improvements in treatment application and efficacy, and the development of more robust therapeutic options may derive from the diverse and complex ecosystem of the gut.

REFERENCES

1. Wilks S (1859) The morbid appearance of the intestine of Miss Banks. *The Medical Times Gazette*.
2. Lukas M, Bortlik M, & Maratka Z (2006) What is the origin of ulcerative colitis? Still more questions than answers. *Postgrad Med J* 82(972):620-625.
3. Langan RC, Gotsch PB, Krafczyk MA, & Skillinge DD (2007) Ulcerative colitis: diagnosis and treatment. *Am Fam Physician* 76(9):1323-1330.
4. da Silva BC, Lyra AC, Rocha R, & Santana GO (2014) Epidemiology, demographic characteristics and prognostic predictors of ulcerative colitis. *World J Gastroenterol* 20(28):9458-9467.
5. Bilsborough J MD, Targan SR (2014) Divide and Conquer: Using Patient Stratification to Optimize Therapeutic Drug Development in Inflammatory Bowel Disease. *Journal of Immunology and clinical research* 2(1).
6. Mahadevan U (2004) Medical treatment of ulcerative colitis. *Clin Colon Rectal Surg* 17(1):7-19.
7. Doherty GA & Cheifetz AS (2009) Management of acute severe ulcerative colitis. *Expert Rev Gastroenterol Hepatol* 3(4):395-405.
8. Cohen RD*, et al.* (2010) Systematic review: the costs of ulcerative colitis in Western countries. *Aliment Pharmacol Ther* 31(7):693-707.
9. De Dombal FT (1968) Ulcerative colitis: definition, historical background, aetiology, diagnosis, naturel history and local complications. *Postgrad Med J* 44(515):684-692.
10. Sartor RB & Mazmanian SK (2012) Intestinal Microbes in Inflammatory Bowel Diseases. *Am J Gastroenterol Suppl* 1(1):15-21.
11. Kruis W*, et al.* (1997) Double-blind comparison of an oral Escherichia coli preparation and mesalazine in maintaining remission of ulcerative colitis. *Aliment Pharmacol Ther* 11(5):853-858.
12. Rembacken BJ, Snelling AM, Hawkey PM, Chalmers DM, & Axon AT (1999) Non-pathogenic Escherichia coli versus mesalazine for the treatment of ulcerative colitis: a randomised trial. *Lancet* 354(9179):635-639.
13. Kruis W*, et al.* (2004) Maintaining remission of ulcerative colitis with the probiotic Escherichia coli Nissle 1917 is as effective as with standard mesalazine. *Gut* 53(11):1617-1623.
14. Bibiloni R*, et al.* (2005) VSL#3 probiotic-mixture induces remission in patients with active ulcerative colitis. *Am J Gastroenterol* 100(7):1539-1546.
15. Ohkusa T*, et al.* (2005) Effectiveness of antibiotic combination therapy in patients with active ulcerative colitis: a randomized, controlled pilot trial with long-term follow-up. *Scand J Gastroenterol* 40(11):1334-1342.
16. Khan KJ*, et al.* (2011) Antibiotic therapy in inflammatory bowel disease: a systematic review and meta-analysis. *Am J Gastroenterol* 106(4):661-673.
17. Ivanov, II*, et al.* (2009) Induction of intestinal Th17 cells by segmented filamentous bacteria. *Cell* 139(3):485-498.
18. Round JL & Mazmanian SK (2010) Inducible Foxp3+ regulatory T-cell development by a commensal bacterium of the intestinal microbiota. *Proc Natl Acad Sci U S A* 107(27):12204-12209.
19. Atarashi K*, et al.* (2011) Induction of colonic regulatory T cells by indigenous Clostridium species. *Science* 331(6015):337-341.
20. von Schillde MA*, et al.* (2012) Lactocepin secreted by lactobacillus exerts anti-inflammatory effects by selectively degrading proinflammatory chemokines. *Cell Host Microbe* 11(4):387-396.

21. Yan F*, et al.* (2011) Colon-specific delivery of a probiotic-derived soluble protein ameliorates intestinal inflammation in mice through an EGFR-dependent mechanism. *J Clin Invest* 121(6):2242-2253.
22. Goto Y*, et al.* (2014) Segmented filamentous bacteria antigens presented by intestinal dendritic cells drive mucosal Th17 cell differentiation. *Immunity* 40(4):594-607.
23. Smith PM*, et al.* (2013) The microbial metabolites, short-chain fatty acids, regulate colonic Treg cell homeostasis. *Science* 341(6145):569-573.
24. Park J*, et al.* (2015) Short-chain fatty acids induce both effector and regulatory T cells by suppression of histone deacetylases and regulation of the mTOR-S6K pathway. *Mucosal Immunol* 8(1):80-93.
25. Furusawa Y*, et al.* (2013) Commensal microbe-derived butyrate induces the differentiation of colonic regulatory T cells. *Nature* 504(7480):446-450.
26. Leppkes M*, et al.* (2009) RORgamma-expressing Th17 cells induce murine chronic intestinal inflammation via redundant effects of IL-17A and IL-17F. *Gastroenterology* 136(1):257-267.
27. Ott SJ*, et al.* (2004) Reduction in diversity of the colonic mucosa associated bacterial microflora in patients with active inflammatory bowel disease. *Gut* 53(5):685-693.
28. Frank DN*, et al.* (2007) Molecular-phylogenetic characterization of microbial community imbalances in human inflammatory bowel diseases. *Proc Natl Acad Sci U S A* 104(34):13780-13785.
29. Morgan XC*, et al.* (2012) Dysfunction of the intestinal microbiome in inflammatory bowel disease and treatment. *Genome Biol* 13(9):R79.
30. Gevers D*, et al.* (2014) The treatment-naive microbiome in new-onset Crohn's disease. *Cell Host Microbe* 15(3):382-392.
31. Qin J*, et al.* (2010) A human gut microbial gene catalogue established by metagenomic sequencing. *Nature* 464(7285):59-65.
32. Langholz E (2010) Current trends in inflammatory bowel disease: the natural history. *Therapeutic advances in gastroenterology* 3(2):77-86.
33. Packey CD & Sartor RB (2008) Interplay of commensal and pathogenic bacteria, genetic mutations, and immunoregulatory defects in the pathogenesis of inflammatory bowel diseases. *Journal of internal medicine* 263(6):597-606.
34. Bibiloni R, Mangold M, Madsen KL, Fedorak RN, & Tannock GW (2006) The bacteriology of biopsies differs between newly diagnosed, untreated, Crohn's disease and ulcerative colitis patients. *Journal of medical microbiology* 55(Pt 8):1141-1149.
35. Uronis JM*, et al.* (2011) Gut microbial diversity is reduced by the probiotic VSL#3 and correlates with decreased TNBS-induced colitis. *Inflamm Bowel Dis* 17(1):289-297.
36. Nagalingam NA, Kao JY, & Young VB (2011) Microbial ecology of the murine gut associated with the development of dextran sodium sulfate-induced colitis. *Inflamm Bowel Dis* 17(4):917-926.
37. Kabeerdoss J, Sankaran V, Pugazhendhi S, & Ramakrishna BS (2013) Clostridium leptum group bacteria abundance and diversity in the fecal microbiota of patients with inflammatory bowel disease: a case-control study in India. *BMC gastroenterology* 13:20.
38. Sokol H*, et al.* (2009) Low counts of Faecalibacterium prausnitzii in colitis microbiota. *Inflammatory bowel diseases* 15(8):1183-1189.
39. Walker AW*, et al.* (2011) High-throughput clone library analysis of the mucosa-associated microbiota reveals dysbiosis and differences between inflamed and non-inflamed regions of the intestine in inflammatory bowel disease. *BMC Microbiol* 11:7.
40. Kumari R, Ahuja V, & Paul J (2013) Fluctuations in butyrate-producing bacteria in ulcerative colitis patients of North India. *World J Gastroenterol* 19(22):3404-3414.

41. Louis P & Flint HJ (2009) Diversity, metabolism and microbial ecology of butyrate-producing bacteria from the human large intestine. *FEMS microbiology letters* 294(1):1-8.
42. Segain JP*, et al.* (2000) Butyrate inhibits inflammatory responses through NFkappaB inhibition: implications for Crohn's disease. *Gut* 47(3):397-403.
43. Sokol H*, et al.* (2008) Faecalibacterium prausnitzii is an anti-inflammatory commensal bacterium identified by gut microbiota analysis of Crohn disease patients. *Proc Natl Acad Sci U S A* 105(43):16731-16736.
44. Okamoto T*, et al.* (2000) Preventive efficacy of butyrate enemas and oral administration of Clostridium butyricum M588 in dextran sodium sulfate-induced colitis in rats. *Journal of gastroenterology* 35(5):341-346.
45. Hudcovic T*, et al.* (2012) Protective effect of Clostridium tyrobutyricum in acute dextran sodium sulphate-induced colitis: differential regulation of tumour necrosis factor-alpha and interleukin-18 in BALB/c and severe combined immunodeficiency mice. *Clin Exp Immunol* 167(2):356-365.
46. Maloy KJ & Powrie F (2011) Intestinal homeostasis and its breakdown in inflammatory bowel disease. *Nature* 474(7351):298-306.
47. Harrison OJ & Maloy KJ (2011) Innate immune activation in intestinal homeostasis. *J Innate Immun* 3(6):585-593.
48. Brandtzaeg P, Carlsen HS, & Halstensen TS (2006) The B-cell system in inflammatory bowel disease. *Adv Exp Med Biol* 579:149-167.
49. Haller D*, et al.* (2010) Guidance for substantiating the evidence for beneficial effects of probiotics: probiotics in chronic inflammatory bowel disease and the functional disorder irritable bowel syndrome. *J Nutr* 140(3):690S-697S.
50. Yui S*, et al.* (2012) Functional engraftment of colon epithelium expanded in vitro from a single adult Lgr5(+) stem cell. *Nat Med* 18(4):618-623.
51. He XW, He XS, Lian L, Wu XJ, & Lan P (2012) Systemic Infusion of Bone Marrow-Derived Mesenchymal Stem Cells for Treatment of Experimental Colitis in Mice. *Dig Dis Sci*.
52. Langille MG*, et al.* (2013) Predictive functional profiling of microbial communities using 16S rRNA marker gene sequences. *Nat Biotechnol* 31(9):814-821.
53. Berry D*, et al.* (2012) Phylotype-level 16S rRNA analysis reveals new bacterial indicators of health state in acute murine colitis. *The ISME journal* 6(11):2091-2106.
54. Vaishnava S, Behrendt CL, Ismail AS, Eckmann L, & Hooper LV (2008) Paneth cells directly sense gut commensals and maintain homeostasis at the intestinal host-microbial interface. *Proc Natl Acad Sci U S A* 105(52):20858-20863.
55. Stappenbeck TS, Hooper LV, & Gordon JI (2002) Developmental regulation of intestinal angiogenesis by indigenous microbes via Paneth cells. *Proc Natl Acad Sci U S A* 99(24):15451-15455.
56. Bansal T, Alaniz RC, Wood TK, & Jayaraman A (2010) The bacterial signal indole increases epithelial-cell tight-junction resistance and attenuates indicators of inflammation. *Proc Natl Acad Sci U S A* 107(1):228-233.
57. Medeiros MR*, et al.* (2011) Antimicrobial activities of indole alkaloids from Tabernaemontana catharinensis. *Nat Prod Commun* 6(2):193-196.
58. Tamaoki J, Kadota J, & Takizawa H (2004) Clinical implications of the immunomodulatory effects of macrolides. *Am J Med* 117 Suppl 9A:5S-11S.
59. Bartosh TJ*, et al.* (2010) Aggregation of human mesenchymal stromal cells (MSCs) into 3D spheroids enhances their antiinflammatory properties. *Proceedings of the National Academy of Sciences of the United States of America* 107(31):13724-13729.
60. Mondel M*, et al.* (2009) Probiotic E. coli treatment mediates antimicrobial human beta-defensin synthesis and fecal excretion in humans. *Mucosal Immunol* 2(2):166-172.

61. Collins MD*, et al.* (1994) The phylogeny of the genus Clostridium: proposal of five new genera and eleven new species combinations. *International journal of systematic bacteriology* 44(4):812-826.
62. Wehkamp J*, et al.* (2005) Reduced Paneth cell alpha-defensins in ileal Crohn's disease. *Proc Natl Acad Sci U S A* 102(50):18129-18134.
63. Garner CD*, et al.* (2009) Perturbation of the small intestine microbial ecology by streptomycin alters pathology in a Salmonella enterica serovar typhimurium murine model of infection. *Infect Immun* 77(7):2691-2702.
64. Meisch JP*, et al.* (2013) Human beta-defensin 3 peptide is increased and redistributed in Crohn's ileitis. *Inflamm Bowel Dis* 19(5):942-953.
65. Bassaganya-Riera J*, et al.* (2012) Probiotic Bacteria Produce Conjugated Linoleic Acid Locally in the Gut That Targets Macrophage PPAR gamma to Suppress Colitis. *PLoS One* 7(2):e31238.
66. Pagnini C*, et al.* (2010) Probiotics promote gut health through stimulation of epithelial innate immunity. *Proc Natl Acad Sci U S A* 107(1):454-459.
67. Zhang Q*, et al.* (2009) Mesenchymal stem cells derived from human gingiva are capable of immunomodulatory functions and ameliorate inflammation-related tissue destruction in experimental colitis. *J Immunol* 183(12):7787-7798.
68. Rojas M*, et al.* (2005) Bone marrow-derived mesenchymal stem cells in repair of the injured lung. *American journal of respiratory cell and molecular biology* 33(2):145-152.
69. Matters GL*, et al.* (2008) The opioid antagonist naltrexone improves murine inflammatory bowel disease. *Journal of immunotoxicology* 5(2):179-187.
70. Ishikura T*, et al.* (2003) Interleukin-18 overproduction exacerbates the development of colitis with markedly infiltrated macrophages in interleukin-18 transgenic mice. *J Gastroenterol Hepatol* 18(8):960-969.
71. Roediger FC*, et al.* (2010) Nucleic acid extraction efficiency and bacterial recovery from maxillary sinus mucosal samples obtained by brushing or biopsy. *Am J Rhinol Allergy* 24(4):263-265.
72. Cox MJ*, et al.* (2010) Airway microbiota and pathogen abundance in age-stratified cystic fibrosis patients. *PLoS One* 5(6):e11044.
73. Hazen TC*, et al.* (2010) Deep-sea oil plume enriches indigenous oil-degrading bacteria. *Science* 330(6001):204-208.
74. Cox MJ*, et al.* (2010) Lactobacillus casei abundance is associated with profound shifts in the infant gut microbiome. *PLoS One* 5(1):e8745.
75. Brodie EL*, et al.* (2006) Application of a high-density oligonucleotide microarray approach to study bacterial population dynamics during uranium reduction and reoxidation. *Appl Environ Microbiol* 72(9):6288-6298.
76. Pielou EC (1966) The measurement of diversity in different types of biological samples. *Journal of Theoretical Biology* 13:131-144.
77. Fujimura KE*, et al.* (2010) Man's best friend? The effect of pet ownership on house dust microbial communities. *J Allergy Clin Immunol* 126(2):410-412, 412 e411-413.
78. Benjamini Y & Hochberg Y (1995) Controlling the False Discovery Rate: A Practical and Powerful Approach to Multiple Testing. *Journal of the Royal Statistical Society. Series B (Methodological)* 57 %6(1):289--300 %&.
79. McLean MH, Dieguez D, Jr., Miller LM, & Young HA (2015) Does the microbiota play a role in the pathogenesis of autoimmune diseases? *Gut* 64(2):332-341.
80. Mar JS*, et al.* (2014) Amelioration of DSS-induced murine colitis by VSL#3 supplementation is primarily associated with changes in ileal microbiota composition. *Gut Microbes* 5(4):494-503.

81. Sellon RK*, et al.* (1998) Resident enteric bacteria are necessary for development of spontaneous colitis and immune system activation in interleukin-10-deficient mice. *Infect Immun* 66(11):5224-5231.
82. Wenzel SE (2012) Asthma phenotypes: the evolution from clinical to molecular approaches. *Nat Med* 18(5):716-725.
83. Akdis CA*, et al.* (2013) Endotypes and phenotypes of chronic rhinosinusitis: a PRACTALL document of the European Academy of Allergy and Clinical Immunology and the American Academy of Allergy, Asthma & Immunology. *J Allergy Clin Immunol* 131(6):1479-1490.
84. Dutta AK & Chacko A (2016) Influence of environmental factors on the onset and course of inflammatory bowel disease. *World J Gastroenterol* 22(3):1088-1100.
85. Neuman MG & Nanau RM (2012) Inflammatory bowel disease: role of diet, microbiota, life style. *Transl Res* 160(1):29-44.
86. Montgomery SM, Morris DL, Pounder RE, & Wakefield AJ (1999) Asian ethnic origin and the risk of inflammatory bowel disease. *Eur J Gastroenterol Hepatol* 11(5):543-546.
87. Walker DG*, et al.* (2013) Ethnicity Differences in Genetic Susceptibility to Ulcerative Colitis: A Comparison of Indian Asians and White Northern Europeans. *Inflamm Bowel Dis*.
88. Yatsunenko T*, et al.* (2012) Human gut microbiome viewed across age and geography. *Nature* 486(7402):222-227.
89. Frank DN*, et al.* (2011) Disease phenotype and genotype are associated with shifts in intestinal-associated microbiota in inflammatory bowel diseases. *Inflamm Bowel Dis* 17(1):179-184.
90. Juyal G*, et al.* (2011) An investigation of genome-wide studies reported susceptibility loci for ulcerative colitis shows limited replication in north Indians. *PLoS One* 6(1):e16565.
91. Trompette A*, et al.* (2014) Gut microbiota metabolism of dietary fiber influences allergic airway disease and hematopoiesis. *Nat Med* 20(2):159-166.
92. Arrieta MC*, et al.* (2015) Early infancy microbial and metabolic alterations affect risk of childhood asthma. *Sci Transl Med* 7(307):307ra152.
93. Lewis JD*, et al.* (2015) Inflammation, Antibiotics, and Diet as Environmental Stressors of the Gut Microbiome in Pediatric Crohn's Disease. *Cell Host Microbe* 18(4):489-500.
94. Walmsley RS, Ayres RC, Pounder RE, & Allan RN (1998) A simple clinical colitis activity index. *Gut* 43(1):29-32.
95. Soga T*, et al.* (2006) Differential metabolomics reveals ophthalmic acid as an oxidative stress biomarker indicating hepatic glutathione consumption. *J Biol Chem* 281(24):16768-16776.
96. Dello SA*, et al.* (2013) Systematic review of ophthalmate as a novel biomarker of hepatic glutathione depletion. *Clin Nutr* 32(3):325-330.
97. Walters JD & Chapman KJ (1995) Polyamines found in gingival fluid enhance the secretory and oxidative function of human polymorphonuclear leukocytes in vitro. *J Periodontal Res* 30(3):167-171.
98. Erez O, Goldstaub D, Friedman J, & Kahana C (2002) Putrescine activates oxidative stress dependent apoptotic death in ornithine decarboxylase overproducing mouse myeloma cells. *Exp Cell Res* 281(1):148-156.
99. Sun CY, Hsu HH, & Wu MS (2013) p-Cresol sulfate and indoxyl sulfate induce similar cellular inflammatory gene expressions in cultured proximal renal tubular cells. *Nephrol Dial Transplant* 28(1):70-78.
100. Schepers E*, et al.* (2007) P-cresylsulphate, the main in vivo metabolite of p-cresol, activates leucocyte free radical production. *Nephrol Dial Transplant* 22(2):592-596.

101. Chang MC*, et al.* (2014) p-Cresol affects reactive oxygen species generation, cell cycle arrest, cytotoxicity and inflammation/atherosclerosis-related modulators production in endothelial cells and mononuclear cells. *PLoS One* 9(12):e114446.
102. Hattori T*, et al.* (2008) G2A plays proinflammatory roles in human keratinocytes under oxidative stress as a receptor for 9-hydroxyoctadecadienoic acid. *J Invest Dermatol* 128(5):1123-1133.
103. Rolin J, Al-Jaderi Z, & Maghazachi AA (2013) Oxidized lipids and lysophosphatidylcholine induce the chemotaxis and intracellular calcium influx in natural killer cells. *Immunobiology* 218(6):875-883.
104. Friedrichs B*, et al.* (1999) 13-HPODE and 13-HODE modulate cytokine-induced expression of endothelial cell adhesion molecules differently. *Biofactors* 9(1):61-72.
105. Henricks PA, Engels F, van der Vliet H, & Nijkamp FP (1991) 9- and 13-hydroxy-linoleic acid possess chemotactic activity for bovine and human polymorphonuclear leukocytes. *Prostaglandins* 41(1):21-27.
106. Moghaddam MF*, et al.* (1997) Bioactivation of leukotoxins to their toxic diols by epoxide hydrolase. *Nat Med* 3(5):562-566.
107. Moran JH, Weise R, Schnellmann RG, Freeman JP, & Grant DF (1997) Cytotoxicity of linoleic acid diols to renal proximal tubular cells. *Toxicol Appl Pharmacol* 146(1):53-59.
108. Totani Y*, et al.* (2000) Leukotoxin and its diol induce neutrophil chemotaxis through signal transduction different from that of fMLP. *Eur Respir J* 15(1):75-79.
109. Huang YH, Schafer-Elinder L, Wu R, Claesson HE, & Frostegard J (1999) Lysophosphatidylcholine (LPC) induces proinflammatory cytokines by a platelet-activating factor (PAF) receptor-dependent mechanism. *Clin Exp Immunol* 116(2):326-331.
110. Qin X, Qiu C, & Zhao L (2014) Lysophosphatidylcholine perpetuates macrophage polarization toward classically activated phenotype in inflammation. *Cell Immunol* 289(1-2):185-190.
111. Young D, Ibuki M, Nakamori T, Fan M, & Mine Y (2012) Soy-derived di- and tripeptides alleviate colon and ileum inflammation in pigs with dextran sodium sulfate-induced colitis. *J Nutr* 142(2):363-368.
112. Hou YC, Chu CC, Ko TL, Yeh CL, & Yeh SL (2013) Effects of alanyl-glutamine dipeptide on the expression of colon-inflammatory mediators during the recovery phase of colitis induced by dextran sulfate sodium. *Eur J Nutr* 52(3):1089-1098.
113. Mistry D & Stockley RA (2010) Gamma-glutamyl transferase: the silent partner? *COPD* 7(4):285-290.
114. Hanigan MH (2014) Gamma-glutamyl transpeptidase: redox regulation and drug resistance. *Adv Cancer Res* 122:103-141.
115. Muraoka S & Miura T (2004) Inhibition of xanthine oxidase by phytic acid and its antioxidative action. *Life Sci* 74(13):1691-1700.
116. Nascimento NR*, et al.* (2006) Inositols prevent and reverse endothelial dysfunction in diabetic rat and rabbit vasculature metabolically and by scavenging superoxide. *Proc Natl Acad Sci U S A* 103(1):218-223.
117. Brocker C, Thompson DC, & Vasiliou V (2012) The role of hyperosmotic stress in inflammation and disease. *Biomol Concepts* 3(4):345-364.
118. Bartnicki P, Zbrog Z, Baj Z, Tchorzewski H, & Luciak M (1997) Myoinositol may be a factor in uremic immune deficiency. *Clin Nephrol* 47(3):197-201.
119. Liao J, Seril DN, Yang AL, Lu GG, & Yang GY (2007) Inhibition of chronic ulcerative colitis associated adenocarcinoma development in mice by inositol compounds. *Carcinogenesis* 28(2):446-454.
120. Fuss IJ*, et al.* (1996) Disparate CD4+ lamina propria (LP) lymphokine secretion profiles in inflammatory bowel disease. Crohn's disease LP cells manifest increased secretion of

IFN-gamma, whereas ulcerative colitis LP cells manifest increased secretion of IL-5. *J Immunol* 157(3):1261-1270.
121. Geremia A, Biancheri P, Allan P, Corazza GR, & Di Sabatino A (2014) Innate and adaptive immunity in inflammatory bowel disease. *Autoimmun Rev* 13(1):3-10.
122. Bamias G, Kaltsa G, & Ladas SD (2011) Cytokines in the pathogenesis of ulcerative colitis. *Discov Med* 11(60):459-467.
123. Li Q*, et al.* (2014) Dysbiosis of gut fungal microbiota is associated with mucosal inflammation in Crohn's disease. *J Clin Gastroenterol* 48(6):513-523.
124. Chehoud C*, et al.* (2015) Fungal Signature in the Gut Microbiota of Pediatric Patients With Inflammatory Bowel Disease. *Inflamm Bowel Dis* 21(8):1948-1956.
125. Zwolinska-Wcislo M*, et al.* (2009) Effect of Candida colonization on human ulcerative colitis and the healing of inflammatory changes of the colon in the experimental model of colitis ulcerosa. *J Physiol Pharmacol* 60(1):107-118.
126. Hogan DA, Vik A, & Kolter R (2004) A Pseudomonas aeruginosa quorum-sensing molecule influences Candida albicans morphology. *Mol Microbiol* 54(5):1212-1223.
127. Sakanaka A, Kuboniwa M, Takeuchi H, Hashino E, & Amano A (2015) Arginine-Ornithine Antiporter ArcD Controls Arginine Metabolism and Interspecies Biofilm Development of Streptococcus gordonii. *J Biol Chem* 290(35):21185-21198.
128. Prindiville TP*, et al.* (2000) Bacteroides fragilis enterotoxin gene sequences in patients with inflammatory bowel disease. *Emerg Infect Dis* 6(2):171-174.
129. Ohkusa T*, et al.* (2009) Commensal bacteria can enter colonic epithelial cells and induce proinflammatory cytokine secretion: a possible pathogenic mechanism of ulcerative colitis. *J Med Microbiol* 58(Pt 5):535-545.
130. Rath HC*, et al.* (1996) Normal luminal bacteria, especially Bacteroides species, mediate chronic colitis, gastritis, and arthritis in HLA-B27/human beta2 microglobulin transgenic rats. *J Clin Invest* 98(4):945-953.
131. Rath HC, Wilson KH, & Sartor RB (1999) Differential induction of colitis and gastritis in HLA-B27 transgenic rats selectively colonized with Bacteroides vulgatus or Escherichia coli. *Infect Immun* 67(6):2969-2974.
132. Jenq RR*, et al.* (2015) Intestinal Blautia Is Associated with Reduced Death from Graft-versus-Host Disease. *Biol Blood Marrow Transplant* 21(8):1373-1383.
133. Miller TL & Wolin MJ (1995) Bioconversion of Cellulose to Acetate with Pure Cultures of Ruminococcus albus and a Hydrogen-Using Acetogen. *Appl Environ Microbiol* 61(11):3832-3835.
134. Walker AW*, et al.* (2011) Dominant and diet-responsive groups of bacteria within the human colonic microbiota. *ISME J* 5(2):220-230.
135. Park SK, Kim MS, Roh SW, & Bae JW (2012) Blautia stercoris sp. nov., isolated from human faeces. *Int J Syst Evol Microbiol* 62(Pt 4):776-779.
136. Shenker BJ, Vitale L, & Slots J (1991) Immunosuppressive effects of Prevotella intermedia on in vitro human lymphocyte activation. *Infect Immun* 59(12):4583-4589.
137. Terao N, Saito S, Hayakawa M, & Abiko Y (1992) Suppressive effect of soluble factor(s) derived from Prevotella loescheii ATCC 15930 on proliferation of human lymphocytes. *Oral Microbiol Immunol* 7(4):230-234.
138. Khokhlova EV*, et al.* (2012) Anti-inflammatory properties of intestinal Bifidobacterium strains isolated from healthy infants. *Microbiol Immunol* 56(1):27-39.
139. Riedel CU*, et al.* (2006) Anti-inflammatory effects of bifidobacteria by inhibition of LPS-induced NF-kappaB activation. *World J Gastroenterol* 12(23):3729-3735.
140. Zhang W*, et al.* (2012) Soluble epoxide hydrolase gene deficiency or inhibition attenuates chronic active inflammatory bowel disease in IL-10(-/-) mice. *Dig Dis Sci* 57(10):2580-2591.

141. Zhang W*, et al.* (2013) Soluble epoxide hydrolase deficiency inhibits dextran sulfate sodium-induced colitis and carcinogenesis in mice. *Anticancer Res* 33(12):5261-5271.
142. Patel KP, Luo FJ, Plummer NS, Hostetter TH, & Meyer TW (2012) The production of p-cresol sulfate and indoxyl sulfate in vegetarians versus omnivores. *Clin J Am Soc Nephrol* 7(6):982-988.
143. O'Shea M, Bassaganya-Riera J, & Mohede IC (2004) Immunomodulatory properties of conjugated linoleic acid. *Am J Clin Nutr* 79(6 Suppl):1199S-1206S.
144. Caporaso JG*, et al.* (2012) Ultra-high-throughput microbial community analysis on the Illumina HiSeq and MiSeq platforms. *ISME J* 6(8):1621-1624.
145. Caporaso JG*, et al.* (2010) QIIME allows analysis of high-throughput community sequencing data. *Nat Methods* 7(5):335-336.
146. Edgar RC (2010) Search and clustering orders of magnitude faster than BLAST. *Bioinformatics* 26(19):2460-2461.
147. DeSantis TZ*, et al.* (2006) Greengenes, a chimera-checked 16S rRNA gene database and workbench compatible with ARB. *Appl Environ Microbiol* 72(7):5069-5072.
148. Caporaso JG*, et al.* (2010) PyNAST: a flexible tool for aligning sequences to a template alignment. *Bioinformatics* 26(2):266-267.
149. Haas BJ*, et al.* (2011) Chimeric 16S rRNA sequence formation and detection in Sanger and 454-pyrosequenced PCR amplicons. *Genome Res* 21(3):494-504.
150. Price MN, Dehal PS, & Arkin AP (2009) FastTree: computing large minimum evolution trees with profiles instead of a distance matrix. *Mol Biol Evol* 26(7):1641-1650.
151. Koljalg U*, et al.* (2013) Towards a unified paradigm for sequence-based identification of fungi. *Mol Ecol* 22(21):5271-5277.
152. Bengtsson-Palme J*, et al.* (2013) Improved software detection and extraction of ITS1 and ITS2 from ribosomal ITS sequences of fungi and other eukaryotes for analysis of environmental sequencing data. *Methods in Ecology and Evolution* 4(10):914-919.
153. Team RC (2015) R: A Language and Environment for Statistical Computing.
154. Lozupone C & Knight R (2005) UniFrac: a new phylogenetic method for comparing microbial communities. *Appl Environ Microbiol* 71(12):8228-8235.
155. Jari Oksanen FGB, Roeland Kindt, Pierre Legendre, Peter R. Minchin, R. B. O'Hara, Gavin L. Simpson, Peter Solymos, M. Henry H. Stevens, and Helene Wagner (2015) vegan: Community Ecology Package.
156. Suzuki R & Shimodaira H (2006) Pvclust: an R package for assessing the uncertainty in hierarchical clustering. *Bioinformatics* 22(12):1540-1542.
157. Romero R*, et al.* (2014) The composition and stability of the vaginal microbiota of normal pregnant women is different from that of non-pregnant women. *Microbiome* 2(1):4.
158. Bates D. M. MM, Bolker B. M., Walker S. C (2015) Fitting Linear Mixed-Effects Models Using {me4. *Journal of Statistical Software* 67.
159. Hooper LV, Stappenbeck TS, Hong CV, & Gordon JI (2003) Angiogenins: a new class of microbicidal proteins involved in innate immunity. *Nat Immunol* 4(3):269-273.
160. Cash HL, Whitham CV, Behrendt CL, & Hooper LV (2006) Symbiotic bacteria direct expression of an intestinal bactericidal lectin. *Science* 313(5790):1126-1130.
161. Laifenfeld D*, et al.* (2012) Early patient stratification and predictive biomarkers in drug discovery and development: a case study of ulcerative colitis anti-TNF therapy. *Adv Exp Med Biol* 736:645-653.
162. Hjortswang H*, et al.* (2003) The influence of demographic and disease-related factors on health-related quality of life in patients with ulcerative colitis. *Eur J Gastroenterol Hepatol* 15(9):1011-1020.
163. Bernklev T*, et al.* (2005) Health-related quality of life in patients with inflammatory bowel disease measured with the short form-36: psychometric assessments and a comparison with general population norms. *Inflamm Bowel Dis* 11(10):909-918.

164. Bolge SC, Waters H, & Piech CT (2010) Self-reported frequency and severity of disease flares, disease perception, and flare treatments in patients with ulcerative colitis: results of a national internet-based survey. *Clin Ther* 32(2):238-245.

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- Al Davis

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