

Composition of the gut microbiota in patients with inflammatory bowel disease in Saudi Arabia: A pilot study

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Abstract

Background: Inflammatory bowel disease (IBD) is a chronic intestinal inflammatory condition attributed to a complex interaction between imbalances in the gut microbiome, environmental conditions, and a deregulated immune response. The aim of the study was to investigate the composition of the gut microbiome of Saudi patients with IBD.

Methods: After obtaining an informed consent, fecal samples were collected from 11 participants with IBD (patients) and 10 healthy individuals (controls). The bacterial components of the microbial population were identified by next-generation sequencing of partial 16S rRNA. Statistically significant dissimilarities were observed between samples for all metrics.

Results: The key finding was three negative bacterial biomarkers, Paraprevotellaceae, the Muribaculaceae families of Bacteroidetes phylum, and the Leuconostocaceae family of Firmicutes phylum, which had a higher relative abundance in healthy individuals compared to IBD patients. It was also found that primary microbiota signatures at certain genera and species levels, including *Prevotella copri*, *Bifidobacterium adolescentis*, *Ruminococcus callidus*, *Coprococcus* sp., *Ruminococcus gnavus*, *Dorea formicigenerans*, *Leuconostoc*, *Dialister*, *Catenibacterium*, *Eubacterium bifforme*, and *Lactobacillus mucosae*, were absent in almost all IBD patients, while *Veillonella dispar* was absent in all healthy individuals.

Conclusions: The results of this study provide an overview of the variations in microbiota diversity present in Saudi IBD patients compared to healthy controls.

Keywords: Inflammatory bowel disease, microbiota, Saudi Arabia

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INTRODUCTION

Inflammatory bowel disease (IBD) is a set of inflammatory conditions involving the gastrointestinal tract. The most common forms are ulcerative colitis (UC) and Crohn's

disease,^[1] which are attributed to a dysregulated immune response owing to an imbalance in the gut microbiome triggered by environmental conditions.^[2] The symptoms

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of IBD include rectal bleeding, diarrhea, weight loss, abdominal pain, and extra-intestinal manifestations. UC mainly involves the colonic mucosa, while CD can affect various parts of the digestive tract, from mouth to the anus. Particular types of environmental exposure and a genetic predisposition to IBD may play a role in the impairment of intestinal immunity, which is considered a hallmark of the disease.^[3-6] Such conditions can result in a fall in the quantity of microorganisms in the intestines and a decrease in microbiota diversity, which can subsequently lead to gut inflammation. Several studies have suggested the presence of a link between defective intestinal homeostasis and low biodiversity of the gut of patients with IBD.^[6-8] In both CD and UC patients, there is often an overall decreased biodiversity resulting in a lower proportion of Firmicutes and an increased proportion of Gammaproteobacteria.^[9,10] Altered proportions of gut microbiota are often observed in patients with CD: *The Roseburia* and *Faecalibacterium* genera of the Lachnospiraceae and Ruminococcaceae families usually decrease in quantity, and *Ruminococcus gnavus* generally increases.^[10,11] Broadly, then, the microbiome plays a central role in the homeostasis and immunity of the gut, making it a potential focus of novel therapies and remedies toward the treatment of IBD.^[1,7]

Studies that have examined the composition of the gut microbiome in Saudi Arabian patients with IBD are scant; thus, this study focuses on the composition of gut microbiota in IBD patients in this region.

MATERIALS AND METHODS

Ethical considerations

This study was approved by the Research Committee at the Unit of Biomedical Ethics complying with international ethical guidelines as set out in the research regulations at the university (reference No. 373-19). An informed consent was obtained from all participants, and the study was carried out according to the Declaration of Helsinki.

Study participants and sample collection

The study participants were recruited from the outpatient IBD clinic at a tertiary care university hospital. Ten healthy individuals were also recruited as controls. Participants were included if they were of Saudi Arabian nationality and agreed to be involved in the study, regardless of age and sex. The mean disease duration was 9.09 ± 7.04 years, (range 1–20 years), and disease extent of CD patients was the ileal region in 33%, colonic in 17%, and ileocolonic in 50%, while the distribution of disease in UC was the rectum in 20%, left-sided colon (up to the splenic flexure) in 40% and pancolitis (extending beyond the hepatic

flexure) in 40%. Patients and controls were excluded if they were pregnant, currently breastfeeding, had used biological medication or antibiotic treatments within two months prior to study commencement [Table 1]. The study participants were provided with detailed information regarding the study, including materials for fecal sample collection and a questionnaire for clinical assessment of disease severity. Patients were included upon receipt of a signed consent form. Fecal samples were collected from the participants using iSWAB microbiome kit (Mawi DNA Technologies, Cat.no. ISM-T-1200-R). Upon collection, the fecal samples were stored at 37°C.

Sampling plan

DNA purification from the fecal samples and ZymoBIOMICS™ Microbial Community Standard DNA was extracted from the human stool samples of 10 healthy controls, 11 IBD patients, and ZymoBIOMICS standard (ZYMO Research, USA) using the Pure link™ microbiome DNA purification kit (Cat.no. A29789; Invitrogen, USA). Sample purity testing was carried out using NanoDrop 7000 Fluorometer (Thermo Fisher Scientific, USA), and sample integrity testing was completed

Table 1: Baseline characteristics of the study participants

Clinical characteristic	IBD patients	Controls
Age (years)	28.91±6.4	32.4±5.9
Gender		
Female, (%)	8 (73%)	5 (50%)
Male (%)	3 (27%)	5 (50%)
Disease duration (years)	9.1±7.0	
Disease activity in UC patients, n (%)		
Remission	0 (0%)	
Mild	1 (20%)	
Moderate	0 (0%)	
Severe	4 (80%)	
Disease activity in CD patients, n (%)		
Remission	3 (50%)	
Mild	1 (17%)	
Moderate	0 (0%)	
Severe	2 (33%)	
UC Locations, n (%)		
E1: Proctitis	1 (20%)	
E2: left-sided	2 (40%)	
E3: Pancolitis	2 (40%)	
CD Locations, n (%)		
L1: Ileal	2 (33%)	
L2: Colonic	1 (17%)	
L3: Ileocolonic	3 (50%)	
Laboratory finding (mean±SD)		
Hemoglobin (%)	11.9±1.9	
C-reactive protein (mg/L)	8.1±9.5	
Albumin (g/dL)	37.9±6.8	
Treatments, n (%)		
Corticosteroids	5 (45%)	
Prednisone	4 (80%)	
Budesonide	1 (20%)	
5-aminosalicylic acid (5-ASA) derivatives	3 (27%)	
Immunosuppressants	4 (36%)	
Azathioprine	4 (100%)	

using 1% agarose gel electrophoresis. The result showed an A260:A280 ratio of 1.8:2.1.

DNA isolation and quality assurance

DNA was extracted from stool samples and mock (which helps prevent misreading the analytic result) using PureLink™ microbiome DNA purification kit. The DNA was isolated from 100 µl of stool samples and eluted in 100 µl volume of elution buffer. Results between 0.7 and 18 ng/µl were used to prepare library sequencing.

Bacterial 16S rRNA gene sequencing

A DNA sample was subjected to polymerase chain reaction (PCR) amplification of the V3–V4 regions of bacterial 16S rRNA, in a total volume of 30 µL, performed using the universal primers 341F 5'-ACTCCTACGGGAGGCAGCAG-3' and 806R 5'-GGACTACHVGGGTWTCTAAT-3'. The PCR program was carried out as follows: initial denaturation at 98°C for 3 min, followed by 30 cycles of 98°C for 45 s, annealing at 55°C for 45 s, extension at 72°C for 45 s, and a final extension at 72°C for 7 min. The PCR products were run on agarose gel (1%) and then gel-purified using a DNA Gel Extraction Kit (QIAGEN, Hilden, Germany) according to the manufacturer's instructions. Next-generation sequencing library construction and high-throughput sequencing using illumine sequencing (MiSeq) were generally used in the microbiome analysis, and these steps were carried out at the Beijing Genomic Institute (BGI) in China to recover ~300 bp (base pair), pair-end reads of the V3 and V4 regions. The ends of each were overlapped to generate high-quality, full-length reads.

Data analysis

A sample size calculation was carried out to determine the probability that the samples were typical.^[11] The raw data was analyzed using the Quantitative Insights Into Microbial Ecology 2 (QIIME, v1.80) bioinformatics tool. Trimmed V3–V4 16S rRNA reads, using Trimmomatic software (Version 0.33) were merged into single sequences using the Fast Length Adjustment of SHort reads (FLASH, Version 1.2.11) software. Merged sequences were filtered to detach low-quality sequences. The latter were reads shorter than 110 nucleotides, truncation of a sequence at any site with a mean quality score of <20 over a 50 bp sliding window, or truncated reads lower than 50 bp. The unique sequence group was linked to tags and classified (using operational taxonomic units (OTUs)) with a 97% identity cut-off using the de novo OTU selection. We kept only OTUs with at least 0.01% mean relative abundance as predominant. The relative abundance values ranked OTUs graphically, on x- and y-axes; then the rank curve was rendered using R software (v3.1.1). Taxonomies

were assigned by the RDP classifier (Version 2.2)^[12] and different databases (GreenGenes, the Ribosomal Database Project, SILVA, the genomic-based 16S rRNA database, and The All-Species Living Tree) with a confidence threshold of 0.7. Chimeric sequences were deleted using Usearch (Version 8.0). Alpha diversity analyses, including observed species, were calculated by Mothur (v1.31.2), using Shannon and Simpson effective. The drawing curve following role-of-three was based on estimating OTU numbers of the extracted tags (in multiples of 500) and detecting the maximum depth (number of reads) permitted to retain all samples in the dataset. Sequences were extracted randomly according to minimum sequence number for all samples, and the extracted sequences formed a new file (OTU table biom). The results were used to calculate beta diversity for measurement of the evolutionary development between species: The bigger the index, the greater the evolutionary difference between samples. Beta diversity heat maps were determined using the tool gplots in the R program (v3.1.1) and drawn by the function aheatmap using non-negative matrix factorization algorithms in R. The distance algorithm was Euclidean, and the clustering method was found to be complete. At the phylum level, all species were used to draw the heat map, and taxa of an abundance of less than 0.5% in all samples were classified as “others.” The values were all log-transformed to minimize the dissimilarity degree between the relative abundance values. The representative sequences were aligned against the SILVA databases (Silva_108_core_aligned_seqs) using PyNAST with the “align_seqs.py” script. A representative OTU phylogenetic tree was constructed using the QIIME (v1.80) built-in scripts, including the FastTree method for phylogenetic tree construction. The tags with the highest abundance of each genus were chosen as the corresponding representative sequences. The genus-level phylogenetic tree was obtained in the same way as the OTU phylogenetic tree. Following this, the phylogeny tree was constructed using the R program (v3.1.1).

Statistical analysis

The results were analyzed using a permutation multivariate analysis of variance (PERMANOVA) to test for significance between values. All statistical tests were two-sided and followed by a Benjamini–Hochberg correction procedure. An adjusted *P* value of <0.05 was set as statistically significant. The Benjamini–Hochberg false discovery rate (FDR) correction was used to correct for multiple hypothesis testing where applicable. Using the Bray–Curtis dissimilarity statistic, weighted and unweighted UniFrac distance metrics were used to identify beta diversity within and between groups,^[13] and plotted with principal coordinate analysis (PCoA), which was performed using the “ade4” package and the R program (v3.1.1). The

boxplot and rarefaction curve were generated using the R software (v3.1.1). Taxa were filtered using the linear discriminant analysis method. Effect size were used to determine the characteristic most likely to appear different among groups, by coupling standard tests for statistical significance with extra tests encoding biological consistency and effect relevance, which was carried out using the Linear discriminant analysis Effect Size^[13] software.^[14]

Data availability

The data have been submitted to National Center for Biotechnology Information (NCBI) under BioProject no. PRJNA673073 (<https://dataview.ncbi.nlm.nih.gov/object/PRJNA673073>) with BioSample identifiers SAMN16591214-SAMN16591234 with accession number SRA16000303-SRA16000323.

RESULTS

Characteristics of the subjects

The study included 11 Saudi IBD patients (six CD and five UC patients) aged 20–41 years, (median age 28.5 years); and 10 healthy controls, aged 20–45 years (median age 34 years). Eight of the patients and five of the controls were females. None of patients or controls were smokers. The mean hemoglobin value for the IBD patients was 11.9 ± 1.9 g/dL, C-reactive protein 8.1 ± 9.5 mg/dL, and the albumin level 37.9 ± 6.8 . The detailed characteristics of the participants are shown in Table 1.

Diversity and rarefaction curve

A description of the observed species detected from OTU annotation is shown in Supplementary Table S1. Differences in the phylotype richness and evenness (α diversity) were detected between controls and IBD patient groups. Patients with IBD showed lower microbial α -diversity and differed significantly from controls, as reflected by the Shannon diversity index ($P < 0.005$) and the Simpson diversity index ($P < 0.024$). The Shannon and Simpson values reflect the species diversity of the communities in terms of both species richness and evenness. However, the Shannon index gives greater weight to sequence richness, while the Simpson index gives greater weight to evenness. With the same species richness, the greater the species evenness reflects greater the community diversity. Alpha diversity per subject indicates a decrease in biodiversity in the patient ostensibly owing to IBD, in terms of Shannon measures. However, almost the converse results were detected in terms of Simpson measures [Figure 1].

To show the difference of OTU distribution in various samples, a principal component analysis (PCA) was used

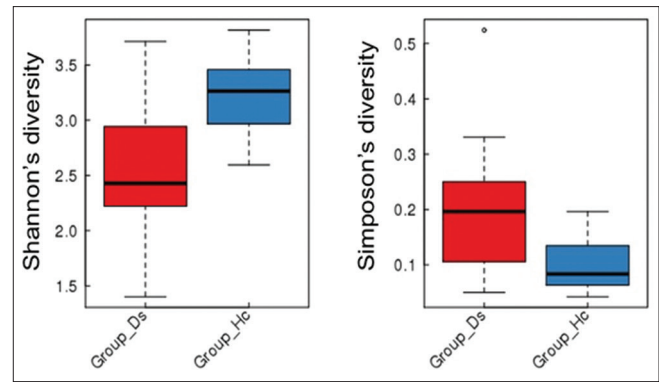


Figure 1: Alpha diversity indices as boxplots to describe richness ($P < 0.005$) and evenness ($P < 0.024$) at the healthy (blue) and patient (red) group level. Hc = Control, Ds = IBD patients

to construct a two-dimensional graph to summarize factors that may be mainly responsible for this difference. The similarity is high if two groups are closely located. Based on the OTU abundance information, each OTU's relative abundance in each sample was calculated, and the principal coordinate analysis (PCoA) of the OTU was carried out with the relative abundance value [Figure 2]. The PCoA plot partially showed a similar tendency in the distances within and between groups. The diversity of IBD patients was higher toward PCoA 2 direction (PC2), whereas healthy subject diversity was higher toward the PCoA 1 direction (PC1). Overall, the diagram showed that the mean value of the IBD group was localized in the positive directions of PCoA 1 and PCoA 2 (PC1 and PC2). By contrast, the healthy control group was localized negatively. These results indicated that the microbiome signatures of the two groups differed, ostensibly owing to IBD. Rarefaction curves based on the number of OTUs or observed species were drawn [Supplementary Figure S1]. The rarefaction measures indicated that the maximum number of sequences reads it used for further analysis of

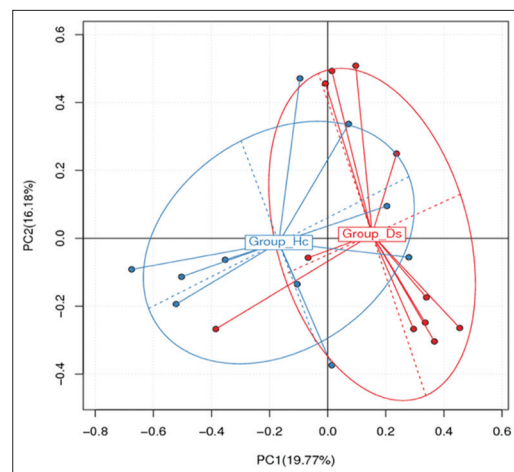


Figure 2: Principal coordinate analysis (PCOS) depends on the total OTUs' abundance of different samples. Hc: Control; Ds: IBD patients

taxonomy abundance is 36,000 [Supplementary Figure S2]. Also, partial least squares discriminant analysis (PLS-DA) was performed to sharpen the separation between groups of observations, by hopefully rotating the principal component analysis (PCA). A maximum separation among groups is obtained to determine which variables carry the separating information. This shows a clear differentiation between the two groups [Supplementary Figure S3].

Gut microbiome at the phyla, family, genera, and species levels

A phylogenetic tree describing taxonomic groups of gut microbiome at the phyla and genera levels is shown in Supplementary Figure S4. The results indicate that the most common phyla are Firmicutes (55 genera), Proteobacteria (19 genera), Bacteroidetes (10 genera), Actinobacteria (9 genera), Euryarchaeota (1 genus), Fusobacteria (1 genus), Lentisphaerae (1 genus), Thermi (1 genus), and Verrucomicrobia (1 genus). The results [Figure 3] indicate that the highly abundant OTUs belong to six of the previously mentioned phyla (e.g., Firmicutes, Bacteroidetes, Proteobacteria, Verrucomicrobia, Fusobacteria, and Actinobacteria). The gut microbiota analysis shows a significant change in the proportion of the two most abundant microbial phyla in healthy controls and IBD patients: Firmicutes and Bacteroidetes. By contrast, the IBD group showed greater abundance of Proteobacteria (15% vs. 32%), Verrucomicrobia (0.52% vs. 0.54%), and Fusobacteria (0.006% vs. 0.1%) and lower quantities of the phyla Firmicutes (46% vs. 37%), Bacteroidetes (35% vs. 30%), and Actinobacteria (2.9% vs. 0.6%). The family levels show 19 significant differences between IBD patients and controls. A considerable increase in the abundance of OTUs was found in the families Bacteroidaceae, Porphyromonadaceae, Verrucomicrobiaceae, Enterobacteriaceae, Streptococcoaceae, Rikenellaceae

Lactobacillaceae, Alcaligenaceae, Fusobacteraceae, and Veillonellaceae, while a statistically significant reduction was shown in Actinomycetaceae, Bifidobacteriaceae, Paraprevotellaceae, Prevotellaceae, Muribaculoceae, Erysipelotrichaceae, Lachnospiraceae, Ruminococcaceae, and Succinivibrionaceae [Supplementary Figure S5]. The highly abundant phyla included 50 genera [Supplementary Figure S6]. The analysis at the genus level also showed differences between IBD individuals and controls. A significant increase in the abundance of OTUs of the genera *Escherichia*, *Bacteroides*, *Sutterella*, *Proteus*, and *Streptococcus* was found, which accounts for more than 1% of the total bacteria. The genera *Bifidobacterium*, *Faecalibacterium*, *Prevotella*, *Eubacterium*, *Coprococcus*, *Dialister*, *Roseburia*, *Ruminococcus*, and *Blautia*, which account for more than 1% of total bacteria, were markedly lower in IBD patients than in healthy controls.

The results identified 38 bacterial species, where Tenericutes (1 phylotype), Verrucomicrobia (1 phylotype), Actinobacteria (3 phylotypes), Proteobacteria (4 phylotypes), Bacteroidetes (7 phylotypes), and Firmicutes (22 phylotypes) had the greatest abundance. The analysis showed a larger number of species with significantly higher abundance in IBD patients, compared with controls. Of these IBD patient biomes, 22 species significantly decreased, 14 species increased, and two species were absent in comparison with healthy controls [Figure 3]. Compared to healthy controls, the most significant increase in species in IBD patients was *Bacteroides fragilis*, *Escherichia coli*, and *Lactobacillus salivarius*, which account for more than 1% of total bacteria in the gut microbiome. The abundance of OTUs with respect to *Faecalibacterium prausnitzii*, *Bacteroides plebeius*, *Bacteroides uniformis*, *Bifidobacterium adolescentis*, *R. gnavus*, *Coprococcus eutactus*, *Prevotella copri*, and *Ruminococcus bromii*, accounts for more than 1% of total bacteria in the microbiome, which

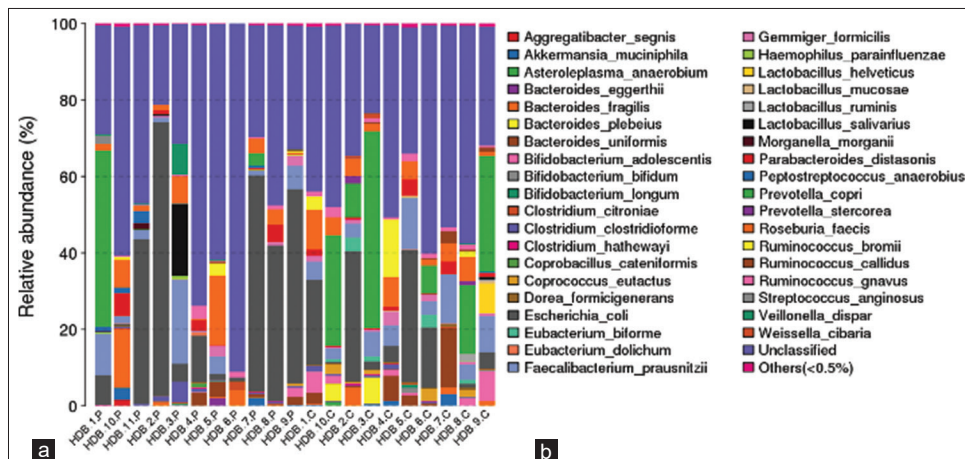


Figure 3: Relative abundance (a) and species (b) level as measured by Metastats at sample and group levels. H = Healthy individuals, P = IBD patients

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was significantly decreased in IBD patients compared to controls.

Significant differences analysis between groups

Linear discriminant analysis Effect Size^[13] was used to determine the features (organisms, clades, operational taxonomic units, genes, and functions) most likely to display differences among groups by coupling standard tests for statistical significance with additional tests to encode biological consistency and effect relevance. The key findings indicate three negative bacterial biomarkers, namely Paraprevotellaceae and the Muribaculaceae families of Bacteroidetes and the Leuconostocaceae family of the Firmicutes, which have a higher relative abundance in healthy individuals compared to IBD patients. There was a decrease in Paraprevotellaceae in IBD patients (average relative abundance in control vs. IBD patients of 0.85% vs. 0.004%, respectively), which corresponds with the succinate-producing bacterium. Also, Muribaculaceae was decreased in IBD patients (average relative abundance 0.43% in controls and 0.045% in IBD patients). There was also a marked decrease in IBD patients in terms of the Leuconostocaceae family (average relative abundance, 0.002% and 0.24% in IBD patients and healthy individuals, respectively) [Figure 4]. Also, other primary signatures (or biomarkers) at the genera and species levels were absent in most IBD patients as shown by a linear discriminant analysis (LDA) [Figure 5]. These include *P. copri* (belonging to the Prevotellaceae family), *B. adolescentis* (belonging to the Bifidobacteriaceae family), *Ruminococcus callidus* (belonging to the Ruminococcaceae family), *Coprococcus sp.*, *R. gnavus*, *D. formicigenerans*, and *Leuconostoc* (belonging to the Lachnospiraceae family), *Dialister sp.* (belonging to the Lachnospiraceae family), *Catenibacterium*, *Eubacterium Biforme* (belonging to the Erysipelotrichaceae family), and *Lactobacillus mucosae* (belonging to the Lactobacillaceae family). By contrast, *Veillonella dispar* (belonging to Veillonellaceae family) was absent in healthy individuals.

DISCUSSION

This study suggests that modification in the gut microbiota is associated with individuals diagnosed with IBD, although the data collected on overall intestinal microbiota change in patients with IBD against healthy controls is limited to Saudi Arabia. Also, while the incidence of IBD seems to be increasing in Saudi Arabia,^[14] an imbalance in the gut microbiome may contribute to changing epidemiology.^[1] In the present study, the next-generation technique was used to investigate gut microbiome composition in Saudi patients with IBD, and these results were compared with internationally published results of various ethnicities and

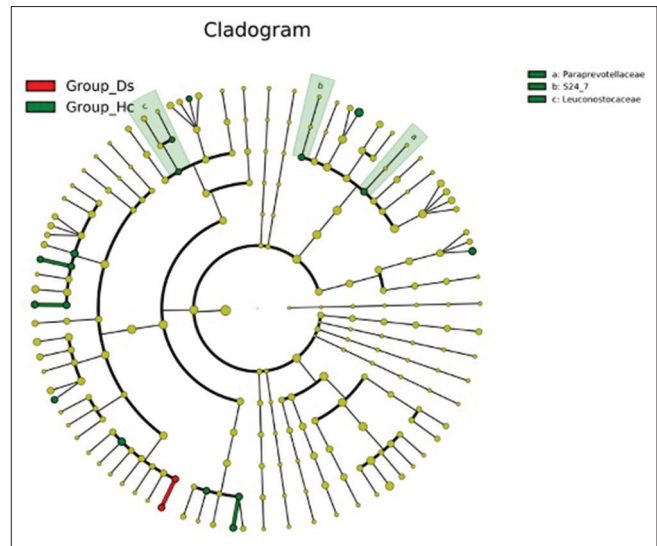


Figure 4: LEfSe tree showing three families statistically significant between healthy individuals and IBD patients. Different colors indicate different groups. LEfSe indicates important microbe biomarkers in the group, and the biomarker name is listed in the upper right corner. Group_Hc = Healthy individuals, group_Ds = IBD patients

races. Many studies have reported a decrease in biodiversity in patients with IBD, known as α diversity, or species richness and evenness, which is reduced in the fecal microbiome in IBD patients compared with healthy individuals. This decreased diversity has contributed to reduced quantity of the dominant taxa, Firmicutes.^[15,16] The results demonstrated a significant difference between the healthy control group and the IBD group, according to PCoA and UniFrac distance analysis; indeed, the data of healthy individuals is consistent with that of Eun *et al.*^[17] The gut microbiota in healthy individuals is dominated by two phyla: Firmicutes (46.2 and 50.0%) and Bacteroidetes (34.60 and 40.00%). The remaining phyla, including Proteobacteria (15.40 and 6.20%) and Actinobacteria (2.90 and 0.85%), tended to be of lower concentrations. However, data of the gut microbiota in IBD patients showed an increase in Proteobacteria (33.00 and 33.81%) and Firmicutes (36.70 and 38.00%) (which includes the *Clostridium* and *Faecalibacterium*), although Bacteroidetes (29.80 and 25.41%) (which includes *Prevotella*) were significantly decreased compared to the controls. The Firmicutes are engaged in short-chain fatty acid and butyrate production. These molecules have a role in gut homeostasis, and the Bacteroidetes are involved in carbohydrate digestion, producing substrates for colonocytes.^[18] The reduction of these two domain phyla of gut bacteriome has been shown in various IBD group studies. Sokol *et al.* (2017) and Quince *et al.* (2015) found that Actinobacteria (mainly *Bifidobacterium*) in IBD patients was depleted.^[8,19] However, some other studies have found that *Bifidobacterium* increased in IBD patients.^[20]

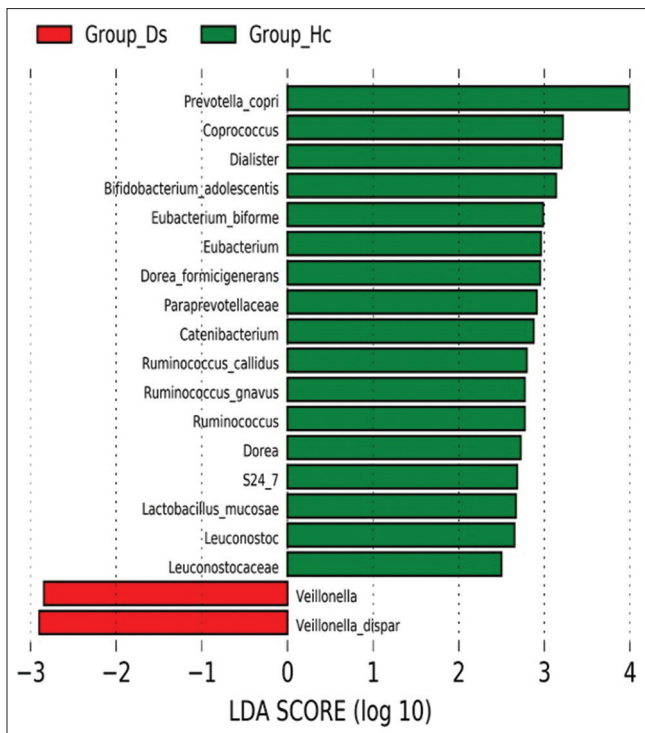


Figure 5: LDA score between healthy (group _Hc) and IBD patients (group_Ds). Distinctive taxa of bacteria with statistically significant differences at the family, genera, and species levels between groups are shown. IBD patients are indicated in red color, and healthy individuals are indicated in green. Group_Hc = Healthy individuals, group_Ds = IBD patients

The present results also show that Fusobacteria significantly increased in the IBD group. By contrast, other studies have indicated that the abundance of Fusobacteria is reduced in IBD patients.^[17] At the family level, we observed a low abundance of some bacterial families of Pasteurellaceae, Lachnospiraceae (including the genera of *Dorea*, *Blautia*, *Anaerostipes*, *Roseburia*, *Coprococcus*), and Ruminococcaceae (including *Ruminococcus* and *Faecalibacterium*). These results broadly correspond with Sokol *et al.*^[21] We also observed an increase in the families of Rikenellaceae, Gemellaceae, Enterobacteriaceae, Eubacteriaceae (including *Eubacterium sp.*) in IBD patients compared to healthy controls.

As indicated above, it was found that IBD affected the human intestinal microbiome with respect to 16 genera and species biomarkers. The overall key signatures (biomarkers) concerned at the genera and species levels were *P. copri* (which is affiliated with the Prevotellaceae family), *B.adolescentis* (which belong to the Bifidobacteriaceae family), *R. callidus* (which belongs to the Ruminococcaceae family), *Coprococcus sp.*, *R. gnavus*, *D. formicigenerans*, and *Leuconostoc sp.* (which belongs to the Lachnospiraceae family), *Dialister sp.* (which is affiliated with the Lachnospiraceae family), *Catenibacterium sp.* and *E. Biforme* (which belong to the

Erysipelotrichaceae family), and *L. mucosae* (which belongs to the Lactobacillaceae family) were virtually absent in all IBD patients. By contrast, *V. dispar* (which belongs to the Veillonellaceae family) was absent in healthy individuals, while IBD patients showed a significant increase in this bacterium. The absence of biomarkers at the genera or species levels in IBD patients or controls may not be surprising at the outset, because this finding has been well documented.^[22] Whether, the absence is an effect or a cause of intestinal inflammation is a fundamental question that remains to be resolved. A number of gut microflora evolve with a complex polysaccharide-rich diet and dietary fermentation, resulting in the production of short-chain fatty acids (SCFAs). SCFAs include propionate, acetate, and butyrate, which represent a primary energy source for colonic epithelial cells,^[23] and preserve them from inflammation.^[24,25] The reduction of dietary fiber correlates with IBD development.^[26,27] Aside from this, a lack of fiber diets is associated with a low concentration of SCFAs.^[27] SCFA-producing bacteria, such as the genera *Coprococcus*,^[28] *Dialister*,^[11] *R. callidus*,^[15] and *E. biforme*,^[29] decreased in IBD patients. Also, lactic acid bacteria, such as the genus *Leuconostoc*, reduced in IBD patients; this genus is particularly well adapted to sugary niches and consequently possesses a broad spectrum of biocatalytic properties useful in carbohydrate modification.^[30] *B. adolescentis* is a species of gram-positive, anaerobic, and folate compound producing bacteria that regulate intestinal homeostasis. Folate (also known as vitamin B9) shares in many metabolic processes that are considered essential for cell division. Folate supplementation is required for patients with IBD owing to its capacity to control rectal cell reproduction and promoting the permanence of Foxp3 regulatory T (Treg) cells, decreasing intestinal inflammation;^[11] this species is a constant resident of the gastrointestinal tract, vagina, and mouth.^[31] *R. gnavus* produces inflammatory polysaccharide, which is known to reduce the production of inflammatory cytokines, such as TNF α by dendritic cells,^[32] while *L. mucosae* protect the host from mucosal inflammation by downregulation of inflammatory cytokines or stimulation of IL-10, an anti-inflammatory cytokine;^[29] *R. gnavus* and *L. Mucosae* populations bloom during flares of symptoms in IBD patients. Also, *P. Copri* and *V. dispar* are gram-negative; *P. copri* promote dextran sulfate sodium-induced colitis in mice, in association with raised IFN- γ production. Thus, *P. copri* enhance Th1 immune response in experimental colitis, while *V. dispar* plays a role in dysmetabolism of bile acids in IBD,^[33] because it is able to degrade cholate and deoxycholate in secondary products; secondary biliary acids are an essential component in pro-inflammatory processes.^[34]

In recent years, one study^[35] has shown a correspondence between ethnicity or population variations and gut microbiome structures. A number of geographically associated divergences in gut microbiome composition contribute to differences in the host immunity and genetics. In other cases, cultural and behavioral features such as diet, hygiene, parasitic load, environmental exposure, etc., are more significant than genetics. This study has examined the gut microbiome of the remote hunter-gatherer community, which is based on starchy diets, including tubers or cassava, nuts, wild game, plants, and honey, with significant quantities of *Prevotella* sp., *Bacteroides* sp., *Bifidobacterium* sp., Proteobacteria, *Ruminobacter* sp. Spirochaetes, and Clostridiales, among others.^[35] Concurrently, the diets of Western (US/European) urban industrialized societies, and those consuming diets high in protein and fatty food, improved sanitation and hygiene practices, and habitual use of antibiotics and other drugs often show a great abundance in Firmicutes.^[36-38]

There are many studies demonstrating geographical or ethnicity-specific factors which might influence intestinal microbiota composition of IBD patients. For instance, the American community,^[34] Saudi population, both Chinese^[39] and Korean communities,^[17] and the European community^[20,21] showed low abundances of Firmicutes, Bacteroidetes, Lachnospiraceae, *Faecalibacterium* sp., *Ruminococcus* sp., and *Eubacteriome* sp., while Proteobacteria was low abundance in IBD patients. On the other hand, they indicated an increase in abundance of *Ruminococcus gnavus* in IBD patients in Europe an (France,^[21] Vevey in Switzerland^[20]) and North American populations,^[34] but it was decreasing in Saudi patients. Also, the Chinese^[39] showed high abundances of *Bifidobacterium* sp., but North American,^[34] Saudi, and European (France^[21]) communities showed low abundance in *Bifidobacterium* sp.

Many studies have pointed out the geographical or ethnicity-specific divergences in human gut microbiota structures. However, the determination of change in the gut microbiota as a cause or consequence of IBD is a complex problem. Still, it is unclear whether IBD is a cause or consequence of microbiome change, although it may be concluded that microbiome changes and IBD are biomarkers of each other.

We acknowledge that the study we present suffers from some limitations such as the small sample size and absence of mucosa-associated microbiota data. Additionally, we recognize that sampling CD patients with different disease distributions separate from UC patients would have provided us with more insights about the microbiota

profile of each disease population. Therefore, larger, well-funded, prospectively designed studies are needed to further validate our observations.

In summary, the results of this study provide an overview of the variations in microbiota diversity present in Saudi IBD patients compared to healthy controls. Further larger studies are needed to validate these findings.

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Conflicts of interest

There are no conflicts of interest.

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SUPPLEMENTARY INFORMATION

Statistics of gut 16S rRNA (V3-V4 region) gene sequence datasets of healthy individuals versus IBD patients

The gut microbiomes composition of IBD patients and non-IBD controls was examined. Illumina MiSeq was used to analyze all 21 fecal samples based on the 16S rRNA (V3-V4 region) gene amplicon sequencing. The statistical analysis of the raw data and its processing are shown in Supplementary Figure S1. A total of 8,420,158 clean sequence reads were generated from stool samples of healthy individuals and IBD patients, with average read numbers of 446,343 and 359,702 per sample, respectively. A total of 8,390,357 tag-linked sequences were from stool samples of healthy individuals and IBD patients with average read numbers of 444,870 and 358,332 per sample, respectively. A total of 1,029,852 sequence tags were generated from stool samples of healthy people and IBD patients, with average read numbers of 45,909 and 51,886 per subject, respectively. Sequence tags were assigned to 622 OTUs (operational taxonomic units) across samples with $\geq 97\%$ similarity. A summation of 3,728 OTUs for the 21 subjects was generated with 177 OTUs per subject, ranging from 65 to 255 OTUs, and averaging 203 and 135 OTUs for healthy individuals and IBD patients, respectively. The results for the number of observed species (number of OTUs) per subject increased in healthy individuals and decreased in patients with IBD.

Supplementary Table S1: OUT taxonomy

OUT Id	Abundn-ce	Taxonomy
Otu573	9	Bacteria;Firmicutes;Clostridia;Clostridiales;Christensenellaceae
Otu486	7	Bacteria;Firmicutes;Clostridia;Clostridiales
Otu487	6	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu488	12	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Anaerotruncus
Otu489	4	Bacteria;Proteobacteria;Alphaproteobacteria;Rhizobiales;Methylobacteriaceae;Methylobacterium
Otu510	2187	Bacteria;Actinobacteria;Actinobacteria;Bifidobacteriales;Bifidobacteriaceae;Bifidobacterium
Otu529	2	Bacteria;Firmicutes;Clostridia;Clostridiales;Christensenellaceae
Otu528	3	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Odoribacteriaceae;Butyricimonas
Otu523	2	Bacteria;Firmicutes;Bacilli
Otu522	60	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae
Otu521	20	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Coprococcus
Otu520	750	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Bacteroidaceae;Bacteroides
Otu527	14	Bacteria;Firmicutes;Clostridia;Clostridiales;Christensenellaceae
Otu526	19	Bacteria;Firmicutes;Clostridia;Clostridiales
Otu525	6	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Ruminococcus
Otu524	4	Bacteria;Proteobacteria;Gammaproteobacteria;Enterobacteriales;Enterobacteriaceae;Providencia
Otu318	45	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu319	41	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Ruminococcus
Otu310	20	Bacteria;Firmicutes;Clostridia;Clostridiales
Otu311	25	Bacteria;Tenericutes;Mollicutes;RF39
Otu312	60	Bacteria;Firmicutes;Clostridia;Clostridiales;Mogibacteriaceae
Otu313	75	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Oscillospira
Otu314	534	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Dorea
Otu315	17	Bacteria;Firmicutes;Clostridia;Clostridiales
Otu316	17	Bacteria;Firmicutes;Clostridia;Clostridiales;Tissierellaceae;ph2
Otu317	97	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Ruminococcus
Otu610	2	Bacteria;Actinobacteria;Coriobacteriia;Coriobacteriales;Coriobacteriaceae
Otu417	9	Bacteria;Firmicutes;Erysipelotrichi;Erysipelotrichales;Erysipelotrichaceae
Otu416	6	Bacteria;Tenericutes;Mollicutes;RF39
Otu415	144	Bacteria;Firmicutes;Clostridia;Clostridiales;Veillonellaceae;Megasphaera
Otu414	23	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu413	12	Bacteria;Firmicutes;Clostridia;Clostridiales;Christensenellaceae
Otu412	12	Bacteria;Firmicutes;Clostridia;Clostridiales
Otu411	13	Bacteria;Firmicutes;Clostridia;Clostridiales;Tissierellaceae;Peptoniphilus
Otu410	14	Bacteria;Firmicutes;Clostridia;Clostridiales
Otu370	29	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Ruminococcus
Otu419	10	Bacteria;Firmicutes;Clostridia;Clostridiales;Christensenellaceae
Otu418	10	Bacteria;Tenericutes;RF3;ML615]-28
Otu371	8	Bacteria;Firmicutes;Erysipelotrichi;Erysipelotrichales;Erysipelotrichaceae
Otu558	2	Bacteria;Firmicutes;Clostridia;Clostridiales;EtOH8
Otu559	2	Bacteria;Firmicutes;Clostridia;Clostridiales
Otu556	282	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Ruminococcus
Otu557	8424	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Bacteroidaceae;Bacteroides
Otu554	3	Bacteria;Firmicutes;Clostridia;Clostridiales;Dehalobacteriaceae;Dehalobacterium

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Table S1: Contd...

OUT Id	Abundn-ce	Taxonomy
Otu555	31	Bacteria;Proteobacteria;Gammaproteobacteria;Enterobacteriales;Enterobacteriaceae;Shigella
Otu552	5	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Ruminococcus
Otu553	12	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu550	1105	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae
Otu551	6	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Ruminococcus
Otu58	3707	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Bacteroidaceae;Bacteroides
Otu59	4103	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae
Otu389	47	Bacteria;Firmicutes;Clostridia;Clostridiales;Mogibacteriaceae
Otu388	10	Bacteria;Firmicutes;Erysipelotrichi;Erysipelotrichales;Erysipelotrichaceae;cc_115
Otu50	2972	Bacteria;Firmicutes;Erysipelotrichi;Erysipelotrichales;Erysipelotrichaceae;Catenibacterium
Otu51	1180	Bacteria;Firmicutes;Clostridia;Clostridiales;Tissierellaceae;Anaerococcus
Otu52	4399	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Coprococcus;Coprococcus_eutactus
Otu53	3457	Bacteria;Firmicutes;Clostridia;Clostridiales;Veillonellaceae;Megasphaera
Otu54	5666	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Ruminococcus;Ruminococcus_gnavus
Otu55	1413	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Coprococcus
Otu56	819	Bacteria;Proteobacteria;Gammaproteobacteria;Pasteurellales;Pasteurellaceae;Aggregatibacter;Aggregatibacter_segns
Otu57	1645	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Bacteroidaceae;Bacteroides
Otu379	31	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Coprococcus
Otu251	50	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Bacteroidaceae;Bacteroides
Otu250	83	Bacteria;Actinobacteria;Actinobacteria;Bifidobacteriales;Bifidobacteriaceae;Bifidobacterium;Bifidobacterium_pseudolongum
Otu253	114	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Oscillospira
Otu252	160	Bacteria;Proteobacteria;Betaproteobacteria;Burkholderiales;Alcaligenaceae;Sutterella
Otu255	58	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu254	45	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu257	67	Bacteria;Firmicutes;Bacilli;Turicibacterales;Turicibacteraceae;Turicibacter
Otu256	47	Bacteria;Actinobacteria;Coriobacteriia;Coriobacteriales;Coriobacteriaceae
Otu259	256	Bacteria;Firmicutes;Clostridia;Clostridiales
Otu258	41	Bacteria;Proteobacteria;Deltaproteobacteria;Desulfovibrionales;Desulfovibrionaceae;Desulfovibrio;Desulfovibrio_D168
Otu589	46	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Porphyromonadaceae;Parabacteroides
Otu396	25	Bacteria;Actinobacteria;Actinobacteria;Actinomycetales;Corynebacteriaceae;Corynebacterium;Corynebacterium_simulans
Otu29	7455	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Ruminococcus
Otu28	6810	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Barnesiellaceae
Otu25	5605	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Bacteroidaceae;Bacteroides;Bacteroides_plebeius
Otu24	5171	Bacteria;Firmicutes;Bacilli;Lactobacillales;Streptococcaceae;Streptococcus
Otu27	11536	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Roseburia
Otu26	6853	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Ruminococcus
Otu21	11130	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Ruminococcus;Ruminococcus_bromii
Otu20	12197	Bacteria;Proteobacteria;Gammaproteobacteria;Enterobacteriales;Enterobacteriaceae;Proteus
Otu23	3617	Bacteria;Firmicutes;Clostridia;Clostridiales;Veillonellaceae;Acidaminococcus
Otu22	2556	Bacteria;Firmicutes;Bacilli;Gemellales;Gemellaceae
Otu174	219	Bacteria;Firmicutes;Bacilli;Lactobacillales;Streptococcaceae;Lactococcus
Otu175	325	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Clostridium
Otu176	160	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Prevotellaceae;Prevotella
Otu177	84	Bacteria;Proteobacteria;Alphaproteobacteria;RF32
Otu170	103	Bacteria;Elusimicrobia;Elusimicrobia;Elusimicrobiales;Elusimicrobiaceae
Otu171	661	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Prevotellaceae;Prevotella;Prevotella_stercorea
Otu172	109	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Paraprevotellaceae
Otu173	163	Bacteria;Proteobacteria;Deltaproteobacteria;Desulfovibrionales;Desulfovibrionaceae;Desulfovibrio
Otu178	86	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;S24-7
Otu179	177	Bacteria;Firmicutes;Clostridia;Clostridiales;Clostridiaceae;Clostridium;Clostridium_perfringens
Otu518	9	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu435	5	Archaea;Euryarchaeota;Methanobacteria;Methanobacteriales;Methanobacteriaceae;Methanobrevibacter
Otu434	6	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu437	7	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu436	8	Bacteria;Firmicutes;Clostridia;Clostridiales;Veillonellaceae;Dialister
Otu431	6	Bacteria;Lentisphaerae;Lentisphaeria;Victivallales;Victivallaceae
Otu430	1246	Bacteria;Firmicutes;Clostridia;Clostridiales
Otu433	8	Bacteria;Firmicutes;Clostridia;Clostridiales;Peptococcaceae
Otu432	1013	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae
Otu268	24	Bacteria;Fusobacteria;Fusobacteriia;Fusobacteriales;Fusobacteriaceae;Fusobacterium
Otu588	10	Bacteria;Firmicutes;Clostridia;Clostridiales;Mogibacteriaceae;Mogibacterium
Otu581	3	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Rikenellaceae
Otu580	42	Bacteria;Firmicutes;Clostridia;Clostridiales;Christensenellaceae

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Table S1: Contd...

OUT Id	Abundn-ce	Taxonomy
Otu583	3	Bacteria;TM7;TM7-3;CW040
Otu582	9	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Barnesiellaceae;Barnesiella;Barnesiella_intestinihominis
Otu585	14	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu584	1444	Bacteria;Firmicutes;Erysipelotrichi;Erysipelotrichales;Erysipelotrichaceae;Eubacterium;Eubacterium_biforme
Otu587	10	Bacteria;Firmicutes;Clostridia;Clostridiales
Otu586	4	Bacteria;Firmicutes;Bacilli;Lactobacillales;Carnobacteriaceae;Granulicatella
Otu512	58	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales
Otu513	112	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Bacteroidaceae;Bacteroides
Otu459	9	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu458	7	Bacteria;Firmicutes;Bacilli;Lactobacillales;Streptococcaceae;Streptococcus;Streptococcus_agalactiae
Otu516	3	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Clostridium;Clostridium_methylpentosum
Otu517	5	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu514	4	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Anaerotruncus
Otu515	411	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Prevotellaceae;Prevotella
Otu453	12	Bacteria;Firmicutes;Clostridia;Clostridiales;Mogibacteriaceae
Otu452	10	Bacteria;Firmicutes;Clostridia;Clostridiales;Peptococcaceae;rc4-4
Otu451	8	Bacteria;Firmicutes;Clostridia;Clostridiales;Dehalobacteriaceae;Dehalobacterium
Otu450	14	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu457	4	Bacteria;Actinobacteria;Coriobacteriia;Coriobacteriales;Coriobacteriaceae
Otu456	4	Bacteria;Proteobacteria;Alphaproteobacteria;RF32
Otu455	9	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Porphyromonadaceae;Parabacteroides
Otu454	6	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu397	8	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Ruminococcus
Otu228	73	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Butyrivibrio;Butyrivibrio_crossotus
Otu229	559	Bacteria;Firmicutes;Bacilli;Lactobacillales;Streptococcaceae;Streptococcus
Otu220	191	Bacteria;Firmicutes;Bacilli;Lactobacillales;Lactobacillaceae;Lactobacillus;Lactobacillus_pontis
Otu221	78	Bacteria;Firmicutes;Erysipelotrichi;Erysipelotrichales;Erysipelotrichaceae;cc_115
Otu222	2156	Bacteria;Proteobacteria;Gammaproteobacteria;Enterobacteriales;Enterobacteriaceae;Citrobacter
Otu223	54	Bacteria;Lentisphaerae;Lentisphaeria;Victivallales;Victivallaceae
Otu224	129	Bacteria;Firmicutes;Clostridia;Clostridiales
Otu225	201	Bacteria;Firmicutes;Clostridia;Clostridiales
Otu226	310	Bacteria;Firmicutes;Clostridia;Clostridiales
Otu227	145	Bacteria;Actinobacteria;Coriobacteriia;Coriobacteriales;Coriobacteriaceae;Eggerthella;Eggerthella_lenta
Otu511	2887	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Ruminococcus;Ruminococcus_gnavus
Otu358	75	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Ruminococcus
Otu359	26	Bacteria;Actinobacteria;Coriobacteriia;Coriobacteriales;Coriobacteriaceae
Otu428	253	Bacteria;Verrucomicrobia;Verrucomicrobiae;Verrucomicrobiales;Verrucomicrobiaceae;Akkermansia;Akkermansia_muciniphila
Otu429	16	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Coprococcus
Otu354	29	Bacteria;Actinobacteria;Coriobacteriia;Coriobacteriales;Coriobacteriaceae;Adlercreutzia
Otu355	11	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu356	53	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu357	19	Bacteria;Firmicutes;Clostridia;Clostridiales;Mogibacteriaceae;Mogibacterium
Otu350	11	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Rikenellaceae;Alistipes;Alistipes_indistinctus
Otu351	79	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae
Otu352	16	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Odoribacteriaceae;Butyrivibrio
Otu353	69	Bacteria;Firmicutes;Erysipelotrichi;Erysipelotrichales;Erysipelotrichaceae;Holdemania
Otu519	11	Bacteria;Actinobacteria;Coriobacteriia;Coriobacteriales;Coriobacteriaceae;Atopobium
Otu129	1876	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Dorea;Dorea_formicigenerans
Otu128	463	Bacteria;Firmicutes;Erysipelotrichi;Erysipelotrichales;Erysipelotrichaceae;Clostridium;Clostridium_amosum
Otu127	200	Bacteria;Firmicutes;Clostridia;Clostridiales;Veillonellaceae;Veillonella
Otu126	241	Bacteria;Actinobacteria;Actinobacteria;Actinomycetales;Actinomycetaceae;Varibaculum
Otu125	468	Bacteria;Firmicutes;Clostridia;Clostridiales
Otu124	283	Bacteria;Firmicutes;Clostridia;Clostridiales;Veillonellaceae;Mitsuokella
Otu123	2096	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Lachnospira
Otu122	518	Bacteria;Firmicutes;Bacilli;Lactobacillales;Lactobacillaceae;Lactobacillus;Lactobacillus_mucosae
Otu121	1327	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Oscillospira
Otu120	503	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Ruminococcus
Otu61	1074	Bacteria;Firmicutes;Clostridia;Clostridiales;Veillonellaceae;Megasphaera
Otu60	2451	Bacteria;Firmicutes;Clostridia;Clostridiales;Veillonellaceae;Acidaminococcus
Otu63	2071	Bacteria;Proteobacteria;Betaproteobacteria;Burkholderiales;Alcaligenaceae;Sutterella
Otu62	987	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Rikenellaceae
Otu65	1052	Bacteria;Firmicutes;Clostridia;Clostridiales;Veillonellaceae;Megamonas
Otu64	1308	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Prevotellaceae;Prevotella
Otu67	846	Bacteria;Firmicutes;Clostridia;Clostridiales;Eubacteriaceae;Anaerofustis
Otu66	739	Bacteria;Firmicutes;Clostridia;Clostridiales;Tissierellaceae;Peptoniphilus
Otu69	1283	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Odoribacteriaceae;Odoribacter

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Table S1: Contd...

OUT Id	Abundn-ce	Taxonomy
Otu68	1080	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Paraprevotellaceae;Prevotella
Otu496	3	Bacteria;Actinobacteria;Actinobacteria;Actinomycetales;Corynebacteriaceae;Corynebacterium
Otu495	14	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Paraprevotellaceae;Prevotella
Otu462	1944	Bacteria;Proteobacteria;Gammaproteobacteria;Enterobacteriales;Enterobacteriaceae;Serratia
Otu463	2643	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Lachnospira
Otu460	6	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu461	11	Bacteria;Firmicutes;Clostridia;Clostridiales
Otu466	3	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Ruminococcus
Otu467	478	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Porphyromonadaceae;Parabacteroides
Otu464	9	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu465	15	Bacteria;Firmicutes;Bacilli;Bacillales;Staphylococcaceae;Staphylococcus;Staphylococcus_aureus
Otu468	14	Bacteria;Proteobacteria;Gammaproteobacteria;Aeromonadales;Succinivibrionaceae;Succinivibrio
Otu469	3	Bacteria;Firmicutes;Clostridia;Clostridiales
Otu549	8	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu548	3	Bacteria;Firmicutes;Bacilli;Bacillales;Bacillaceae
Otu545	7	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales
Otu544	52	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae
Otu547	31	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Prevotellaceae;Prevotella
Otu546	8	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Barnesiellaceae;Barnesiella;Barnesiella_intestinihominis
Otu541	2	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu540	4	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu543	4	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu542	36	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Rikenellaceae
Otu608	81	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu609	3	Bacteria;Proteobacteria;Deltaproteobacteria;Desulfobibrionales;Desulfobibrionaceae
Otu602	13	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu603	8	Bacteria;Firmicutes;Clostridia;Clostridiales;Christensenellaceae
Otu600	39	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Prevotellaceae;Prevotella
Otu601	6	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Porphyromonadaceae;Porphyromonas
Otu606	3	Bacteria;Firmicutes;Bacilli;Lactobacillales;Lactobacillaceae;Lactobacillus
Otu607	2	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Ruminococcus
Otu604	4	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Anaerotruncus
Otu605	3	Bacteria;Proteobacteria;Betaproteobacteria;Burkholderiales;Alcaligenaceae
Otu611	9	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Bacteroidaceae;Bacteroides
Otu307	1889	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Porphyromonadaceae;Parabacteroides
Otu306	23	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu305	33	Bacteria;Firmicutes;Clostridia;Clostridiales;Christensenellaceae
Otu304	156	Bacteria;Firmicutes;Clostridia;Clostridiales;Mogibacteriaceae
Otu303	37	Bacteria;Firmicutes;Erysipelotrichi;Erysipelotrichales;Erysipelotrichaceae;Coprobaillus
Otu269	99	Bacteria;Firmicutes;Clostridia;Clostridiales
Otu301	23	Bacteria;Actinobacteria;Coriobacteriia;Coriobacteriales;Coriobacteriaceae
Otu300	131	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae
Otu264	110	Bacteria;Firmicutes;Bacilli;Lactobacillales;Lactobacillaceae;Lactobacillus
Otu265	50	Bacteria;Firmicutes;Bacilli;Lactobacillales;Streptococcaceae;Lactococcus;Lactococcus_garvieae
Otu266	47	Bacteria;Proteobacteria;Deltaproteobacteria;Desulfobibrionales;Desulfobibrionaceae;Desulfobibrion
Otu267	11822	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Ruminococcus
Otu260	180	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Butyricicoccus;Butyricicoccus_pullicaeorum
Otu261	132	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Prevotellaceae;Prevotella
Otu262	82	Bacteria;Firmicutes;Erysipelotrichi;Erysipelotrichales;Erysipelotrichaceae;Clostridium;Clostridium_spiroforme
Otu308	54	Bacteria;Proteobacteria;Betaproteobacteria;Burkholderiales;Oxalobacteraceae;Oxalobacter;Oxalobacter_formigenes
Otu116	11893	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Blautia
Otu117	1129	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu114	1703	Bacteria;Firmicutes;Clostridia;Clostridiales;Clostridiaceae;Clostridium
Otu115	436	Bacteria;Firmicutes;Clostridia;Clostridiales;Tissierellaceae;Finegoldia
Otu112	1203	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu113	257	Bacteria;Firmicutes;Clostridia;Clostridiales
Otu110	294	Bacteria;Firmicutes;Clostridia;Clostridiales;Tissierellaceae;Peptoniphilus
Otu111	1371	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Bacteroidaceae;Bacteroides
Otu118	804	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Oscillospira
Otu119	13326	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Prevotellaceae;Prevotella;Prevotella_copri
Otu286	53	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Odoribacteraceae;Butyricimonas
Otu287	36	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Porphyromonadaceae;Porphyromonas
Otu284	185	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu285	26	Bacteria;Bacteroidetes
Otu282	54	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Coproccoccus

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Table S1: Contd...

OUT Id	Abundn-ce	Taxonomy
Otu283	21	Bacteria;Firmicutes;Clostridia;Clostridiales;Christensenellaceae
Otu280	148	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu281	32	Bacteria;Firmicutes;Erysipelotrichi;Erysipelotrichales;Erysipelotrichaceae
Otu288	31	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Rikenellaceae
Otu289	60	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu38	1630	Bacteria;Firmicutes;Bacilli;Lactobacillales;Streptococcaceae;Streptococcus;Streptococcus_anguinosus
Otu39	3586	Bacteria;Firmicutes;Clostridia;Clostridiales;Peptostreptococcaceae;Peptostreptococcus;Peptostreptococcus_anaerobius
Otu36	2994	Bacteria;Firmicutes;Bacilli;Lactobacillales;Enterococcaceae;Enterococcus
Otu37	5971	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Clostridium;Clostridium_clostridioforme
Otu34	5704	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Gemmiger;Gemmiger_formicilis
Otu35	4290	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae
Otu32	3541	Bacteria;Firmicutes;Clostridia;Clostridiales;Veillonellaceae;Dialister
Otu33	2480	Bacteria;Firmicutes;Clostridia;Clostridiales;Veillonellaceae;Dialister
Otu30	5048	Bacteria;Verrucomicrobia;Verrucomicrobiae;Verrucomicrobiales;Verrucomicrobiaceae;Akkermansia;Akkermansia_muciniphila
Otu31	13352	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Porphyromonadaceae;Parabacteroides;Parabacteroides_distasonis
Otu163	98	Bacteria;Cyanobacteria;4C0d-2;YS2
Otu162	99	Bacteria;Firmicutes;Clostridia;Clostridiales
Otu161	129	Bacteria;Firmicutes;Clostridia;Clostridiales;Christensenellaceae
Otu160	239	Bacteria;Firmicutes;Clostridia;Clostridiales;Christensenellaceae
Otu167	114	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu309	25	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu165	308	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu164	244	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Ruminococcus
Otu169	509	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Clostridium;Clostridium_symbiosum
Otu263	67	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Rikenellaceae
Otu615	123	Bacteria;Firmicutes;Clostridia;Clostridiales;Veillonellaceae
Otu83	591	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Paraprevotellaceae;Prevotella
Otu82	468	Bacteria;Firmicutes;Erysipelotrichi;Erysipelotrichales;Erysipelotrichaceae;Coprobaillus;Coprobaillus_cateniformis
Otu81	1036	Bacteria;Actinobacteria;Actinobacteria;Bifidobacteriales;Bifidobacteriaceae;Bifidobacterium;Bifidobacterium_bifidum
Otu80	1621	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Paraprevotellaceae;Prevotella
Otu87	1085	Bacteria;Firmicutes;Bacilli;Lactobacillales;Lactobacillaceae;Lactobacillus;Lactobacillus_ruminis
Otu86	534	Bacteria;Fusobacteria;Fusobacteriia;Fusobacteriales;Fusobacteriaceae;Fusobacterium
Otu85	2129	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Odoribacteraceae;Odoribacter
Otu84	938	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu89	983	Bacteria;Firmicutes;Clostridia;Clostridiales;Peptostreptococcaceae
Otu88	2105	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Anaerostipes
Otu426	6	Bacteria;Proteobacteria;Epsilonproteobacteria;Campylobacteriales;Campylobacteraceae;Campylobacter
Otu617	4	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae
Otu427	6	Bacteria;Tenericutes;Mollicutes;RF39
Otu424	13	Bacteria;Firmicutes;Clostridia;Clostridiales;Christensenellaceae
Otu501	5	Bacteria;Proteobacteria;Alphaproteobacteria;RF32
Otu500	6	Bacteria;Cyanobacteria;Chloroplast;Streptophyta
Otu503	5	Bacteria;Tenericutes;RF3;ML615J-28
Otu425	11	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Ruminococcus
Otu505	2	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Ruminococcus
Otu504	9	Bacteria;Proteobacteria;Deltaproteobacteria;Desulfovibrionales;Desulfovibrionaceae
Otu507	210	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Prevotellaceae;Prevotella
Otu506	11	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Prevotellaceae;Prevotella
Otu509	20	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Prevotellaceae;Prevotella
Otu422	34	Bacteria;Firmicutes;Clostridia;Clostridiales;Christensenellaceae
Otu423	6	Bacteria;Actinobacteria;Actinobacteria;Actinomycetales;Corynebacteriaceae;Corynebacterium
Otu420	31	Bacteria;Firmicutes;Clostridia;Clostridiales
Otu421	7	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Odoribacteraceae;Butyricimonas
Otu480	3	Bacteria;Tenericutes;Mollicutes;RF39
Otu481	885	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Clostridium;Clostridium_clostridioforme
Otu482	12	Bacteria;Firmicutes;Clostridia;Clostridiales;Mogibacteriaceae
Otu483	48	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Ruminococcus
Otu484	6	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Ruminococcus
Otu485	5	Bacteria;Proteobacteria;Alphaproteobacteria;Rhizobiales;Methylobacteriaceae;Methylobacterium
Otu338	32	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu339	18	Bacteria;Firmicutes;Clostridia;Clostridiales;Tissierellaceae;Peptoniphilus
Otu336	31	Bacteria;Actinobacteria;Coriobacteriia;Coriobacteriales;Coriobacteriaceae

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Table S1: Contd...

OUT Id	Abundn-ce	Taxonomy
Otu337	11	Bacteria;Bacteroidetes;Sphingobacteriia;Sphingobacteriales;Sphingobacteriaceae
Otu334	43	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu335	24	Bacteria;Actinobacteria;Coriobacteriia;Coriobacteriales;Coriobacteriaceae
Otu332	44	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Anaerotruncus
Otu333	35	Bacteria;Firmicutes;Clostridia;Clostridiales;Mogibacteriaceae
Otu330	26	Bacteria;Firmicutes;Bacilli;Lactobacillales;Streptococcaceae;Streptococcus
Otu331	15	Bacteria;Firmicutes;Clostridia;Clostridiales
Otu349	11	Bacteria;Proteobacteria;Deltaproteobacteria;Desulfovibrionales;Desulfovibrionaceae
Otu348	14	Bacteria;Firmicutes;Clostridia;Clostridiales;Tissierellaceae;Peptoniphilus
Otu439	12	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu438	12	Bacteria;Firmicutes;Bacilli;Lactobacillales;Lactobacillaceae;Lactobacillus
Otu343	30	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Prevotellaceae;Prevotella
Otu342	15	Bacteria;Proteobacteria;Alphaproteobacteria;RF32
Otu341	46	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae
Otu340	35	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Oscillospira
Otu347	12	Bacteria;Cyanobacteria;4C0d-2;YS2
Otu346	12	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Bacteroidaceae;Bacteroides
Otu345	13	Bacteria;Actinobacteria;Coriobacteriia;Coriobacteriales;Coriobacteriaceae
Otu344	25	Bacteria;Proteobacteria;Alphaproteobacteria;Rickettsiales;mitochondria
Otu158	114	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Prevotellaceae;Prevotella
Otu159	523	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Paraprevotellaceae;Paraprevotella
Otu152	126	Bacteria;Proteobacteria;Betaproteobacteria;Burkholderiales;Comamonadaceae;Comamonas
Otu153	550	Bacteria;Proteobacteria;Betaproteobacteria;Burkholderiales;Alcaligenaceae;Sutterella
Otu150	198	Bacteria;Firmicutes;Erysipelotrichi;Erysipelotrichales;Erysipelotrichaceae;Bulleidia;Bulleidia_p-1630-c5
Otu151	205	Bacteria;Firmicutes;Clostridia;Clostridiales;Tissierellaceae;WAL_1855D
Otu156	409	Bacteria;Firmicutes;Clostridia;Clostridiales;Veillonellaceae;Phascolarctobacterium
Otu157	646	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Coprococcus
Otu154	251	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu155	1033	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae
Otu72	1378	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Rikenellaceae
Otu73	1948	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;S24-7
Otu70	3374	Bacteria;Firmicutes;Erysipelotrichi;Erysipelotrichales;Erysipelotrichaceae;Eubacterium;Eubacterium_biforme
Otu71	7797	Bacteria;Proteobacteria;Gammaproteobacteria;Enterobacteriales;Enterobacteriaceae
Otu76	6020	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Blautia
Otu77	771	Bacteria;Firmicutes;Bacilli;Lactobacillales;Leuconostocaceae;Weissella;Weissella_cibaria
Otu74	1130	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Prevotellaceae;Prevotella
Otu75	2614	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Bacteroidaceae;Bacteroides
Otu563	3	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales
Otu78	562	Bacteria;Firmicutes;Erysipelotrichi;Erysipelotrichales;Erysipelotrichaceae;Asteroleplasma;Asteroleplasma_anaerobium
Otu79	746	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Prevotellaceae;Prevotella;Prevotella_stercorea
Otu562	5	Bacteria;Tenericutes;Mollicutes;RF39
Otu237	85	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Barnesiellaceae
Otu236	49	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu235	1891	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Clostridium;Clostridium_citroniae
Otu234	395	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Prevotellaceae;Prevotella;Prevotella_copri
Otu233	650	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Rikenellaceae
Otu232	62	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae
Otu231	360	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu230	1082	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae
Otu378	9	Bacteria;Firmicutes;Clostridia;Clostridiales
Otu239	55	Bacteria;Firmicutes;Clostridia;Clostridiales
Otu238	154	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Oscillospira
Otu569	2	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Oscillospira
Otu568	5	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Prevotellaceae;Prevotella
Otu612	60	Bacteria;Firmicutes;Clostridia;Clostridiales;Veillonellaceae;Megamonas
Otu166	299	Bacteria;Firmicutes;Clostridia;Clostridiales
Otu168	1389	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Clostridium;Clostridium_hathewayi
Otu8	8990	Bacteria;Firmicutes;Clostridia;Clostridiales;Veillonellaceae;Megasphaera
Otu9	16226	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Bacteroidaceae;Bacteroides;Bacteroides_uniformis
Otu6	5731	Bacteria;Proteobacteria;Gammaproteobacteria;Aeromonadales;Succinivibrionaceae;Succinivibrio
Otu7	56642	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Faecalibacterium;Faecalibacterium_prausnitzii
Otu4	15267	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Bacteroidaceae;Bacteroides;Bacteroides_fragilis
Otu5	9169	Bacteria;Firmicutes;Bacilli;Lactobacillales;Lactobacillaceae;Lactobacillus;Lactobacillus_salivarius
Otu2	105369	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Bacteroidaceae;Bacteroides
Otu3	76516	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Prevotellaceae;Prevotella;Prevotella_copri

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Table S1: Contd...

OUT Id	Abundn-ce	Taxonomy
Otu1	213730	Bacteria;Proteobacteria;Gammaproteobacteria;Enterobacteriales;Enterobacteriaceae;Escherichia;Escherichia_coli
Otu387	4551	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Prevotellaceae;Prevotella;Prevotella_copri
Otu386	10	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu385	18	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Ruminococcus
Otu471	214	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae
Otu470	3	Bacteria;Lentisphaerae;Lentisphaeria;Victivallales;Victivallaceae
Otu473	27	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Prevotellaceae;Prevotella;Prevotella_copri
Otu384	17	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu475	6	Bacteria;Verrucomicrobia;Opitutae;Cerasiococcales;Cerasiococcaceae
Otu474	4	Bacteria;Firmicutes;Bacilli;Bacillales;Bacillaceae;Bacillus;Bacillus_foraminis
Otu477	3735	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae
Otu476	6	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu479	67	Bacteria;Firmicutes;Clostridia;Clostridiales
Otu383	23	Bacteria;Firmicutes;Clostridia;Clostridiales;Christensenellaceae
Otu382	19	Bacteria;Tenericutes;Mollicutes;RF39
Otu578	2	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Ruminococcus
Otu579	4	Bacteria;Actinobacteria;Actinobacteria;Actinomycetales;Corynebacteriaceae;Corynebacterium
Otu381	358	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Prevotellaceae;Prevotella;Prevotella_copri
Otu570	4	Bacteria;Firmicutes;Clostridia;Clostridiales;Clostridiaceae;Clostridium
Otu571	5	Bacteria;Proteobacteria;Gammaproteobacteria;Enterobacteriales;Enterobacteriaceae
Otu572	8	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Prevotellaceae;Prevotella
Otu380	9	Bacteria;Firmicutes;Clostridia;Clostridiales;Tissierellaceae;1-68
Otu574	3	Bacteria;Firmicutes;Bacilli;Lactobacillales;Lactobacillaceae;Lactobacillus;Lactobacillus_paralimentarius
Otu575	12	Bacteria;Firmicutes;Erysipelotrichi;Erysipelotrichales;Erysipelotrichaceae
Otu576	7	Bacteria;Firmicutes;Erysipelotrichi;Erysipelotrichales;Erysipelotrichaceae
Otu577	5	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;S24-7
Otu619	4	Bacteria;Actinobacteria;Coriobacteriia;Coriobacteriales;Coriobacteriaceae;Adlercreutzia
Otu618	4	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu208	1037	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Prevotellaceae;Prevotella;Prevotella_copri
Otu209	279	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Odoribacteraceae;Butyricimonas
Otu206	59	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Barnesiellaceae
Otu207	86	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Porphyromonadaceae;Parabacteroides
Otu204	408	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Oscillospira
Otu205	170	Bacteria;Firmicutes;Bacilli;Lactobacillales;Carnobacteriaceae;Granulicatella
Otu202	330	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae
Otu203	224	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Coprococcus
Otu200	662	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae
Otu201	119	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu620	5	Bacteria;Firmicutes;Clostridia;Clostridiales;Veillonellaceae;Megasphaera
Otu372	1920	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Bacteroidaceae;Bacteroides
Otu373	27	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Paraprevotellaceae;Prevotella
Otu279	36	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu278	172	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Ruminococcus
Otu376	39	Bacteria;Firmicutes;Clostridia;Clostridiales;Mogibacteriaceae
Otu377	1721	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae
Otu374	23	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu375	10	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu273	80	Bacteria;Proteobacteria;Betaproteobacteria;Burkholderiales;Alcaligenaceae;Sutterella
Otu272	38	Bacteria;Firmicutes;Erysipelotrichi;Erysipelotrichales;Erysipelotrichaceae;Coprobaillus
Otu271	46	Bacteria;Proteobacteria;Gammaproteobacteria;Pseudomonadales;Pseudomonadaceae;Pseudomonas;Pseudomonas_fragi
Otu270	131	Bacteria;Firmicutes;Clostridia;Clostridiales;Veillonellaceae;Dialister
Otu277	342	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Bacteroidaceae;Bacteroides
Otu276	101	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Odoribacteraceae;Butyricimonas
Otu275	34	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Oscillospira
Otu274	50	Bacteria;Firmicutes;Clostridia;Clostridiales
Otu105	367	Bacteria;Firmicutes;Clostridia;Clostridiales
Otu104	2187	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae
Otu107	453	Bacteria;Firmicutes;Bacilli;Lactobacillales;Leuconostocaceae;Leuconostoc
Otu106	1817	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Prevotellaceae;Prevotella;Prevotella_copri
Otu101	997	Bacteria;Actinobacteria;Actinobacteria;Bifidobacteriales;Bifidobacteriaceae;Bifidobacterium;Bifidobacterium_longum
Otu100	900	Bacteria;Proteobacteria;Gammaproteobacteria;Enterobacteriales;Enterobacteriaceae;Morganella;Morganella_morganii
Otu103	1179	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Oscillospira
Otu102	754	Bacteria;Firmicutes;Clostridia;Clostridiales

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Table S1: Contd...

OUT Id	Abundn-ce	Taxonomy
Otu109	412	Bacteria;Firmicutes;Erysipelotrichi;Erysipelotrichales;Erysipelotrichaceae;Eubacterium;Eubacterium_dolichum
Otu108	266	Bacteria;Firmicutes;Erysipelotrichi;Erysipelotrichales;Erysipelotrichaceae;Bulleidia;Bulleidia_moorei
Otu295	56	Bacteria;Firmicutes;Clostridia;Clostridiales;Christensenellaceae
Otu294	33	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae
Otu297	25	Bacteria;Firmicutes;Clostridia;Clostridiales
Otu296	116	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae
Otu291	35	Bacteria;Firmicutes;Clostridia;Clostridiales;Tissierellaceae;Anaerococcus
Otu290	31	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu293	326	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales
Otu292	1665	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae
Otu299	21	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Coprococcus
Otu298	185	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae
Otu497	12	Bacteria;Actinobacteria;Actinobacteria;Actinomycetales;Actinomycetaceae;Actinomyces
Otu198	267	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Porphyromonadaceae;Parabacteroides
Otu199	189	Bacteria;Firmicutes;Bacilli;Lactobacillales;Lactobacillaceae;Lactobacillus;Lactobacillus_zeae
Otu196	128	Bacteria;Tenericutes;Mollicutes;RF39
Otu197	100	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Barnesiellaceae
Otu194	220	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Oscillospira
Otu195	256	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu192	83	Bacteria;Firmicutes;Clostridia;Clostridiales
Otu193	124	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Ruminococcus
Otu190	169	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Oscillospira
Otu191	65	Bacteria;Actinobacteria;Coriobacteriia;Coriobacteriales;Coriobacteriaceae
Otu494	6	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Ruminococcus
Otu493	8	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Ruminococcus
Otu492	9	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu491	11	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu490	17	Bacteria;Firmicutes;Clostridia;Clostridiales;Christensenellaceae;Christensenella
Otu98	977	Bacteria;Firmicutes;Clostridia;Clostridiales;Veillonellaceae;Mitsuokella
Otu99	889	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Coprococcus;Coprococcus_catus
Otu94	2642	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Gemmiger;Gemmiger_formicillis
Otu95	493	Bacteria;Firmicutes;Clostridia;Clostridiales;Tissierellaceae;Parvimonas
Otu96	1295	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Coprococcus
Otu97	685	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae
Otu90	3881	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Coprococcus
Otu91	2475	Bacteria;Firmicutes;Clostridia;Clostridiales;Veillonellaceae;Dialister
Otu92	576	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales
Otu93	1921	Bacteria;Firmicutes;Erysipelotrichi;Erysipelotrichales;Erysipelotrichaceae
Otu538	322	Bacteria;Firmicutes;Clostridia;Clostridiales
Otu539	7	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Oscillospira
Otu534	38	Bacteria;Actinobacteria;Actinobacteria;Actinomycetales;Actinomycetaceae;Actinomyces
Otu535	417	Bacteria;Proteobacteria;Betaproteobacteria;Burkholderiales;Alcaligenaceae;Sutterella
Otu536	121	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Roseburia
Otu537	11	Bacteria;Firmicutes;Clostridia;Clostridiales;Veillonellaceae
Otu530	107	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Prevotellaceae;Prevotella;Prevotella_copri
Otu531	213	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Prevotellaceae;Prevotella
Otu532	3	Bacteria;Firmicutes;Clostridia;Clostridiales;Christensenellaceae
Otu533	4	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Lachnoanaerobaculum;Lachnoanaerobaculum_orale
Otu329	11	Bacteria;Cyanobacteria;4C0d-2;YS2
Otu328	19	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu499	17	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu498	6	Bacteria;Firmicutes;Erysipelotrichi;Erysipelotrichales;Erysipelotrichaceae;cc_115
Otu325	12	Bacteria;Actinobacteria;Coriobacteriia;Coriobacteriales;Coriobacteriaceae
Otu324	13	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;S24-7
Otu327	33	Bacteria;Firmicutes;Clostridia;Clostridiales;Veillonellaceae;Dialister
Otu326	23	Bacteria;Firmicutes;Clostridia;Clostridiales;Peptococcaceae
Otu321	63	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Oscillospira
Otu320	23	Bacteria;Lentisphaerae;Lentisphaeria;Victivallales;Victivallaceae
Otu323	61	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu322	13	Bacteria;Firmicutes;Clostridia;Clostridiales;Veillonellaceae;Dialister
Otu302	47	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Ruminococcus
Otu408	13	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Oscillospira
Otu409	13	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Ruminococcus
Otu400	23	Bacteria;Firmicutes;Clostridia;Clostridiales;Mogibacteriaceae
Otu401	16	Bacteria;Actinobacteria;Actinobacteria;Actinomycetales;Micrococcaceae;Rothia;Rothia_mucilaginosa

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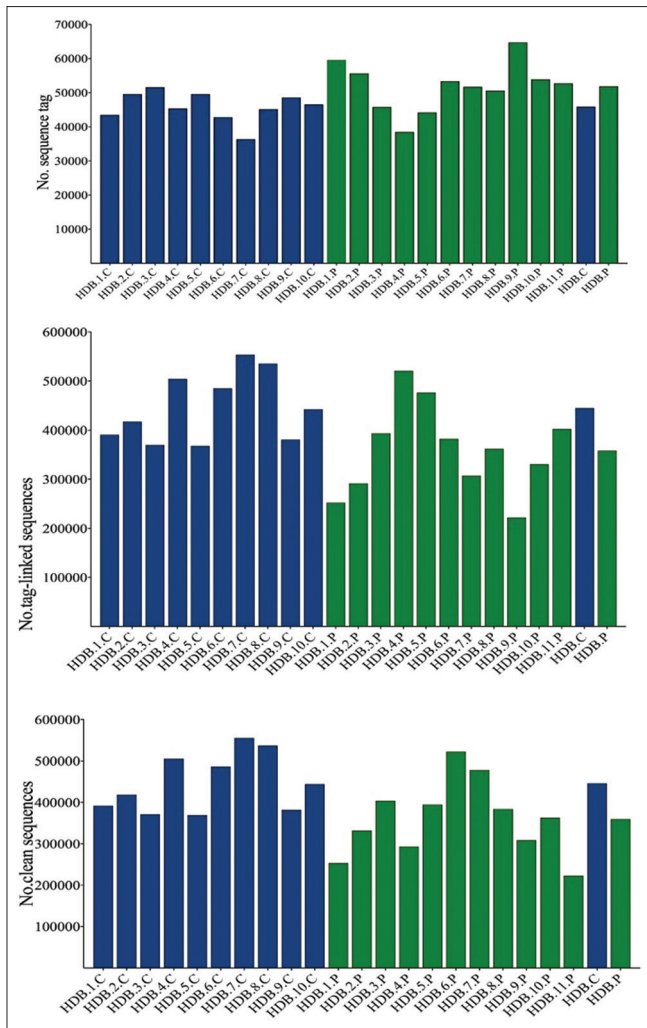
Table S1: Contd...

OUT Id	Abundn-ce	Taxonomy
Otu402	21	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Coprococcus
Otu403	21	Bacteria;Firmicutes;Clostridia;Clostridiales;Christensenellaceae
Otu404	8	Bacteria;Firmicutes
Otu405	32	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae
Otu406	11	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Prevotellaceae;Prevotella
Otu407	65	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Oscillospira
Otu 149	588	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Oscillospira
Otu 148	176	Bacteria;Proteobacteria;Alphaproteobacteria;RF32
Otu 141	1193	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae
Otu 140	633	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Dorea
Otu 143	615	Bacteria;Proteobacteria;Deltaproteobacteria;Desulfovibrionales;Desulfovibrionaceae;Bilophila
Otu 142	213	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Ruminococcus
Otu 145	324	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae
Otu 144	174	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu 147	226	Bacteria;Firmicutes;Clostridia;Clostridiales
Otu 146	1214	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Butyricoccus;Butyricoccus_pullicaeorum
Otu390	18	Bacteria;Firmicutes;Bacilli;Lactobacillales;Lactobacillaceae;Lactobacillus;Lactobacillus_plantarum
Otu391	33	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu392	35	Bacteria;Firmicutes;Clostridia;Clostridiales;Christensenellaceae
Otu393	7	Bacteria;Lentisphaerae;Lentisphaeria;Victivallales;Victivallaceae;Victivallis;Victivallis_vadensis
Otu394	15	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Ruminococcus
Otu395	1679	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Prevotellaceae;Prevotella;Prevotella_copri
Otu49	4091	Bacteria;Firmicutes;Clostridia;Clostridiales;Veillonellaceae;Veillonella;Veillonella_dispar
Otu48	3600	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Lachnospira
Otu47	2341	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Ruminococcus
Otu46	2603	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Ruminococcus;Ruminococcus_callidus
Otu45	1203	Bacteria;Proteobacteria;Alphaproteobacteria;RF32
Otu44	1775	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Ruminococcus
Otu43	1976	Bacteria;Actinobacteria;Actinobacteria;Actinomycetales;Actinomycetaceae;Actinomyces
Otu42	3245	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu41	3810	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Rikenellaceae
Otu40	1898	Bacteria;Firmicutes;Clostridia;Clostridiales
Otu242	70	Bacteria;Firmicutes;Clostridia;Clostridiales;Mogibacteriaceae
Otu243	95	Bacteria;Tenericutes;Mollicutes;RF39
Otu240	161	Bacteria;Actinobacteria;Coriobacteria;Coriobacteriales;Coriobacteriaceae
Otu241	36	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Ruminococcus;Ruminococcus_albus
Otu246	191	Bacteria;Firmicutes;Clostridia;Clostridiales;Mogibacteriaceae
Otu247	139	Bacteria;Firmicutes;Clostridia;Clostridiales
Otu244	3217	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Bacteroidaceae;Bacteroides
Otu245	156	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Rikenellaceae
Otu248	39	Bacteria;Tenericutes;Mollicutes;RF39
Otu249	39	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Odoribacteraceae;Butyricimonas
Otu472	3	Bacteria;Thermi;Deinococci;Deinococcales;Deinococcaceae;Deinococcus
Otu478	3	Bacteria;Proteobacteria;Alphaproteobacteria
Otu598	2	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu599	6	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae
Otu592	3	Bacteria;Firmicutes;Clostridia;Clostridiales;Christensenellaceae
Otu593	3	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu590	5	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Ruminococcus
Otu591	4	Bacteria;Firmicutes;Clostridia;Clostridiales
Otu596	26	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Ruminococcus
Otu597	377	Bacteria;Firmicutes;Clostridia;Clostridiales;Veillonellaceae;Megamonas
Otu594	19	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales
Otu595	41	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae
Otu502	10	Bacteria;Firmicutes;Clostridia;Clostridiales;Veillonellaceae;Dialister
Otu567	2	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu566	5	Bacteria;Firmicutes;Clostridia;Clostridiales;Veillonellaceae
Otu565	5	Bacteria;Firmicutes;Bacilli;Lactobacillales;Lactobacillaceae;Lactobacillus;Lactobacillus_agilis
Otu564	365	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae
Otu448	743	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae
Otu449	21	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Butyricoccus;Butyricoccus_pullicaeorum
Otu561	231	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu560	54	Bacteria;Firmicutes;Clostridia;Clostridiales
Otu444	7	Bacteria;Actinobacteria;Actinobacteria;Actinomycetales;Actinomycetaceae;Mobiluncus
Otu445	6	Bacteria;Firmicutes;Clostridia;Clostridiales
Otu446	13	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu447	2770	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Dorea

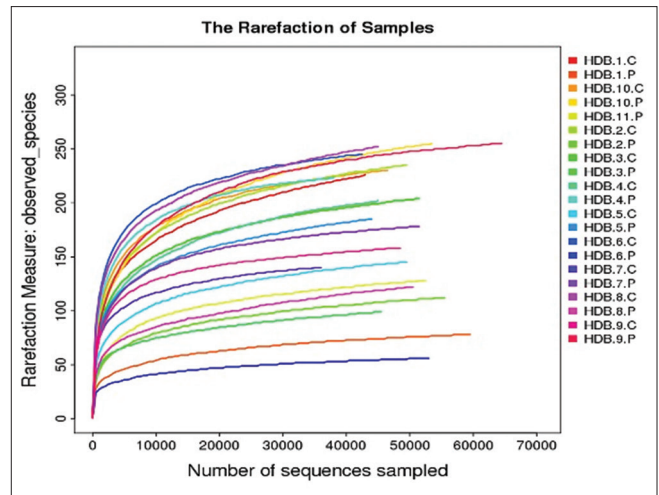
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Table S1: Contd...

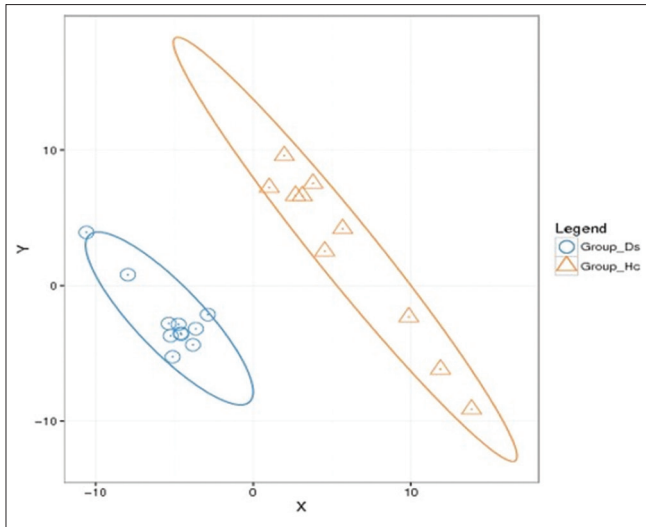
OUT Id	Abundn-ce	Taxonomy
Otu440	9	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu441	159	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Coprococcus
Otu442	28	Bacteria;Firmicutes;Clostridia;SHA-98
Otu443	15	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Ruminococcus
Otu508	10	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Defluviitalea;Defluviitalea_saccharophila
Otu219	78	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Prevotellaceae;Prevotella
Otu218	159	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu215	840	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Bacteroidaceae;Bacteroides;Bacteroides_eggerthii
Otu214	142	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Prevotellaceae;Prevotella
Otu217	202	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Ruminococcus
Otu216	155	Bacteria;Firmicutes;Erysipelotrichi;Erysipelotrichales;Erysipelotrichaceae;Eubacterium;Eubacterium_dolichum
Otu211	149	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu210	145	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Rikenellaceae;Alistipes;Alistipes_indistinctus
Otu213	198	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;S24-7
Otu212	51	Bacteria;Cyanobacteria;4COd-2;YS2
Otu398	31	Bacteria;Firmicutes;Clostridia;Clostridiales;Veillonellaceae;Dialister
Otu399	10	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu361	20	Bacteria;Proteobacteria;Epsilonproteobacteria;Campylobacteriales;Campylobacteraceae;Campylobacter
Otu360	10	Bacteria;Actinobacteria;Coriobacteriia;Coriobacteriales;Coriobacteriaceae
Otu363	24	Bacteria;Firmicutes;Clostridia;Clostridiales;Mogibacteriaceae
Otu362	129	Bacteria;Firmicutes;Clostridia;Clostridiales;Veillonellaceae;Megasphaera
Otu365	14	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu364	2271	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Bacteroidaceae;Bacteroides
Otu367	2157	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Bacteroidaceae;Bacteroides
Otu366	9	Bacteria;Firmicutes;Clostridia;Clostridiales
Otu369	221	Bacteria;Firmicutes;Clostridia;Clostridiales;Veillonellaceae
Otu368	20	Bacteria;Firmicutes;Clostridia;Clostridiales;Dehalobacteriaceae;Dehalobacterium
Otu613	3	Bacteria;Firmicutes;Clostridia;Clostridiales;Peptococcaceae;Peptococcus
Otu621	65	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu130	196	Bacteria;Proteobacteria;Alphaproteobacteria;RF32
Otu131	268	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu132	732	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae;Ruminococcus
Otu133	350	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Ruminococcus;Ruminococcus_gnavus
Otu134	230	Bacteria;Firmicutes;Clostridia;Clostridiales
Otu135	2482	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Coprococcus
Otu136	284	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Prevotellaceae;Prevotella
Otu137	557	Bacteria;Firmicutes;Clostridia;Clostridiales;Clostridiaceae
Otu138	302	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Prevotellaceae;Prevotella
Otu139	1054	Bacteria;Proteobacteria;Gammaproteobacteria;Pasteurellales;Pasteurellaceae;Haemophilus;Haemophilus_para-influenzae
Otu614	2	Bacteria;Proteobacteria;Alphaproteobacteria;Sphingomonadales;Sphingomonadaceae;Sphingopyxis;Sphingopyxis_alaskensis
Otu14	9656	Bacteria;Proteobacteria;Betaproteobacteria;Burkholderiales;Alcaligenaceae;Sutterella
Otu15	3228	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Porphyromonadaceae;Dysgonomonas
Otu16	9110	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Blautia
Otu17	7515	Bacteria;Firmicutes;Clostridia;Clostridiales;Veillonellaceae;Phascolarctobacterium
Otu10	44046	Bacteria;Firmicutes;Clostridia;Clostridiales;Lachnospiraceae;Roseburia;Roseburia_faecis
Otu11	3966	Bacteria;Firmicutes;Bacilli;Lactobacillales;Lactobacillaceae;Lactobacillus;Lactobacillus_helveticus
Otu12	10600	Bacteria;Actinobacteria;Actinobacteria;Bifidobacteriales;Bifidobacteriaceae;Bifidobacterium;Bifidobacterium_adolescentis
Otu13	6305	Bacteria;Firmicutes;Clostridia;Clostridiales;Veillonellaceae;Dialister
Otu616	2	Bacteria;Firmicutes;Bacilli;Lactobacillales;Aerococcaceae;Facklamia
Otu18	7023	Bacteria;Firmicutes;Clostridia;Clostridiales;Veillonellaceae;Dialister
Otu19	7480	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Porphyromonadaceae;Parabacteroides
Otu189	106	Bacteria;Firmicutes;Clostridia;Clostridiales;Tissierellaceae;Peptoniphilus
Otu188	141	Bacteria;Firmicutes;Clostridia;Clostridiales
Otu622	13	Bacteria;Firmicutes;Clostridia;Clostridiales;Veillonellaceae;Acidaminococcus
Otu185	104	Bacteria;Firmicutes;Clostridia;Clostridiales;Ruminococcaceae
Otu184	126	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Bacteroidaceae;Bacteroides
Otu187	148	Bacteria;Tenericutes;Mollicutes;RF39
Otu186	73	Bacteria;Proteobacteria;Epsilonproteobacteria;Campylobacteriales;Campylobacteraceae;Campylobacter;Campylobacter_ureolyticus
Otu181	169	Bacteria;Firmicutes;Clostridia;Clostridiales
Otu180	145	Bacteria;Tenericutes;Mollicutes;RF39
Otu183	620	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales;Odoribacteraceae;Butyricimonas
Otu182	118	Bacteria;Bacteroidetes;Bacteroidia;Bacteroidales



Supplementary Figure S1: Comparison among numbers of clean and tagged sequences and the recovered sequence tags at the sample and group levels for healthy individuals (blue) and patients with IBD. HDB.C: Healthy individuals; HDB.P: Patients with IBD



Supplementary Figure S2: Number of observed species between healthy individuals and IBD patients as rarefaction measures to describe the maximum depth permitted to retain all subjects in the dataset to study relative taxonomic abundance. The arrow indicates the suitable sample size for analyzing taxonomy abundance (36,000 sequence reads). HDB.C = Control, HDB.P = IBD patients



Supplementary Figure S3: Partial least square discriminant analysis (PLS-DA) based on OTUs abundance. Hc = Healthy, Ds = IBD patients



Supplementary Figure S4: Genus level phylogenetic tree of the gut microbiome. Genera of the same phylum are specified by the same color

