Dynamics of the human gut microbiome in Inflammatory Bowel Disease

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Supplementary Information

Supplementary Video 1. Dynamics of healthy controls and IBD subtypes within ordinated UniFrac space. This video illustrates the dynamics along a "healthy plane" for healthy controls. By contrast, the IBD subjects move in a 3rd dimension away from the healthy plane. The extent of this deviation from the healthy plane is quantified and significant for the different IBD subtypes (data shown in Figure 2).

Legend for Supplementary Video 1.

- 🟨 ICD_r
- 🟥 ICD_nr
- 🟪 CCD
- 🟩 HC
- 🟦 UC

Supplementary Dataset 1. Clinical metadata for patients and samples. This QIIME compatible mapping file lists the genetic and clinical context of each sample used in this study. It is available on Qiita as study 1629 and is linked to the online version of the paper at www.nature.com/nmicrobiol

Supplementary Table 1. Summary of the patient cohort

Collected samples				Samples used in downstream analysis		
Category	**Patients**	**Samples**		**Category**	**Patients**	**Samples**
Healthy Controls	9	62		Healthy Controls	7	32
Colonic Crohn's Disease	18	94		Colonic Crohn's Disease	11	44
Ileal Crohn's Disease, non-resected	6	32		Ileal Crohn's Disease, non-resected	4	16
Ileal Crohn's Disease, resected	25	125		Ileal Crohn's Disease, resected	15	60
Ulcerative colitis	60	324		Ulcerative colitis	32	168
Collagenous colitis	15	36		Collagenous colitis	-	-
Lymphocytic colitis	4	10		Lymphocytic colitis	-	-
Total	**137**	**683**		**Total**	**69**	**267**
Female	79	378		Female	36	144
Male	58	305		Male	33	132

Supplementary Table 2. Clinical features of the Random Forests model

Model	CCD	HC	ICD_nr	ICD_r	UC	Mean Decrease in Accuracy	Feature
OTUs and clinical metadata. Accuracy: 66.6%	-0.68	2.42	-2.07	10.70	5.26	10.44	Distance to the Healthy Plane
	0.52	0.00	1.00	-1.55	0.23	0.14	BMI
	0.00	1.00	0.00	-0.69	0.00	0.00	sex
	-1.71	0.98	-1.00	1.75	-3.13	-1.03	f-calprotectin
With Genetic Load Scores (GLS) Accuracy: 68%	2.07	3.20	-1.08	11.15	7.61	11.52	Distance to the Healthy Plane
	0.35	2.89	-1.38	2.81	6.73	5.87	Genetic Load Scores
	1.00	0.00	0.00	0.25	1.41	1.13	sex
	-0.33	0.73	1.27	-0.08	-2.17	-1.44	f-calprotectin
	-1.12	-1.18	0.71	-1.84	-0.85	-1.77	BMI

Clinical and microbial features as predicted by the Random Forests model, with and without the addition of Genetic Load Scores.

Supplementary Table 3. Top features of the Random Forests model

Model	CCD	HC	ICD_nr	ICD_r	UC	Mean Decrease in Accuracy	Feature Name or Taxonomy					
OTUs and clinical metadata. Accuracy: 66.6%	-0.68	2.42	-2.07	10.70	5.26	10.44	Distance to the Healthy Plane					
	0.19	0.73	-0.54	8.98	3.95	8.79	Proteobacteria	Gammaproteobacteria	Alteromonadales	[Chromatiaceae]	[Unassigned]	[Unassigned]
	4.03	-0.22	1.34	5.08	7.50	7.66	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	[Unassigned]	[Unassigned]
	0.11	1.10	-1.29	8.61	-0.20	7.55	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	[Unassigned]	[Unassigned]
	0.74	2.18	-1.28	7.79	2.64	7.42	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	Clostridium	[Unassigned]
	0.24	0.41	0.00	8.46	-0.35	7.29	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	[Unassigned]	[Unassigned]
	0.70	-0.87	-0.33	7.42	1.24	6.79	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Lachnospira	[Unassigned]
	-0.17	1.49	-0.58	7.13	0.29	6.76	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	[Unassigned]	[Unassigned]
	-1.15	6.77	0.00	2.46	4.27	6.26	Firmicutes	Clostridia	Clostridiales	[Unassigned]	[Unassigned]	[Unassigned]
	3.33	-0.58	-2.61	6.42	3.20	5.97	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	[Unassigned]	[Unassigned]
	-0.31	-0.51	-1.00	6.68	0.53	5.81	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	[Unassigned]	[Unassigned]
	0.64	-1.93	-1.31	4.83	5.00	5.67	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	[Unassigned]	[Unassigned]
	0.03	1.78	1.34	4.79	3.32	5.17	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	[Unassigned]	[Unassigned]
	1.02	-2.72	1.34	5.12	3.17	5.06	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Oscillospira	[Unassigned]
	-0.36	2.31	0.76	6.02	1.50	5.06	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	[Unassigned]	[Unassigned]
	-0.52	1.72	1.67	5.33	1.89	5.04	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	[Unassigned]	[Unassigned]
With Genetic Load Scores (GLS) Accuracy: 68%	2.07	3.20	-1.08	11.15	7.61	11.52	Distance to the Healthy Plane					
	-0.18	1.97	-2.72	8.82	-2.58	7.94	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	[Unassigned]	[Unassigned]
	4.77	-0.72	1.00	5.62	7.10	7.68	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	[Unassigned]	[Unassigned]
	-0.89	1.78	-0.63	8.15	1.19	7.62	Proteobacteria	Gammaproteobacteria	Alteromonadales	[Chromatiaceae]	[Unassigned]	[Unassigned]
	1.98	0.53	-0.32	7.93	2.62	7.52	Firmicutes	Clostridia	Clostridiales	Clostridiaceae	Clostridium	[Unassigned]
	-0.07	0.78	-1.57	7.55	-0.26	6.97	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	[Unassigned]	[Unassigned]
	-2.86	7.25	1.00	2.27	4.71	6.84	Firmicutes	Clostridia	Clostridiales	[Unassigned]	[Unassigned]	[Unassigned]
	-0.47	1.30	1.45	7.04	1.53	6.32	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	[Unassigned]	[Unassigned]
	-0.28	-0.07	-0.58	7.25	1.32	6.28	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	Lachnospira	[Unassigned]
	0.07	-1.57	-1.04	6.95	2.87	6.28	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	Oscillospira	[Unassigned]
	-0.02	-1.75	0.63	5.68	6.04	6.14	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	[Unassigned]	[Unassigned]
	-1.48	-1.36	-1.00	7.06	1.42	6.01	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	[Unassigned]	[Unassigned]
	0.35	2.89	-1.38	2.81	6.73	5.87	Genetic Load Score					

	-0.07	0.50	0.00	4.75	4.20	5.29	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	[Unassigned]	[Unassigned]
	0.73	-0.68	-1.34	5.44	3.20	5.28	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	[Unassigned]	[Unassigned]
	-1.87	0.99	-1.73	6.08	0.73	5.24	Firmicutes	Clostridia	Clostridiales	Ruminococcaceae	[Unassigned]	[Unassigned]
	0.54	2.94	1.64	4.13	3.54	5.04	Firmicutes	Clostridia	Clostridiales	Lachnospiraceae	[Unassigned]	[Unassigned]

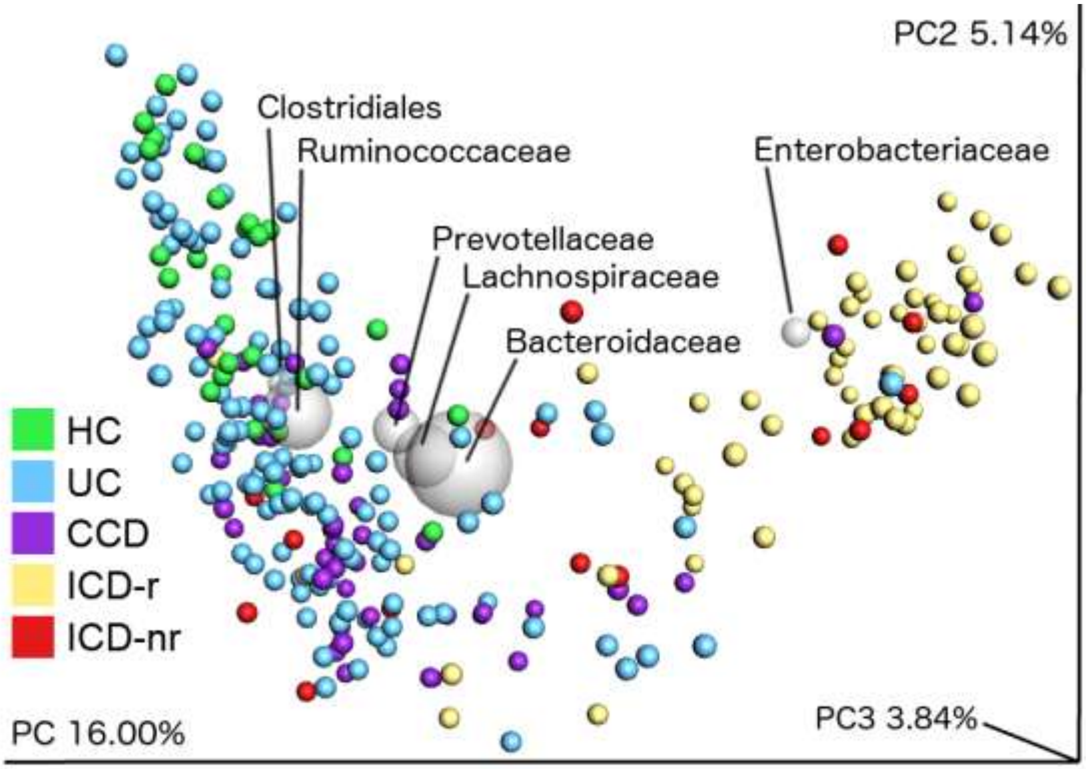
Clinical and microbial features are shown that were predicted by the Random Forests model to decrease cumulative accuracy by at least 5% if permuted.

Supplementary Table 4. Power Analysis for differential abundance tests

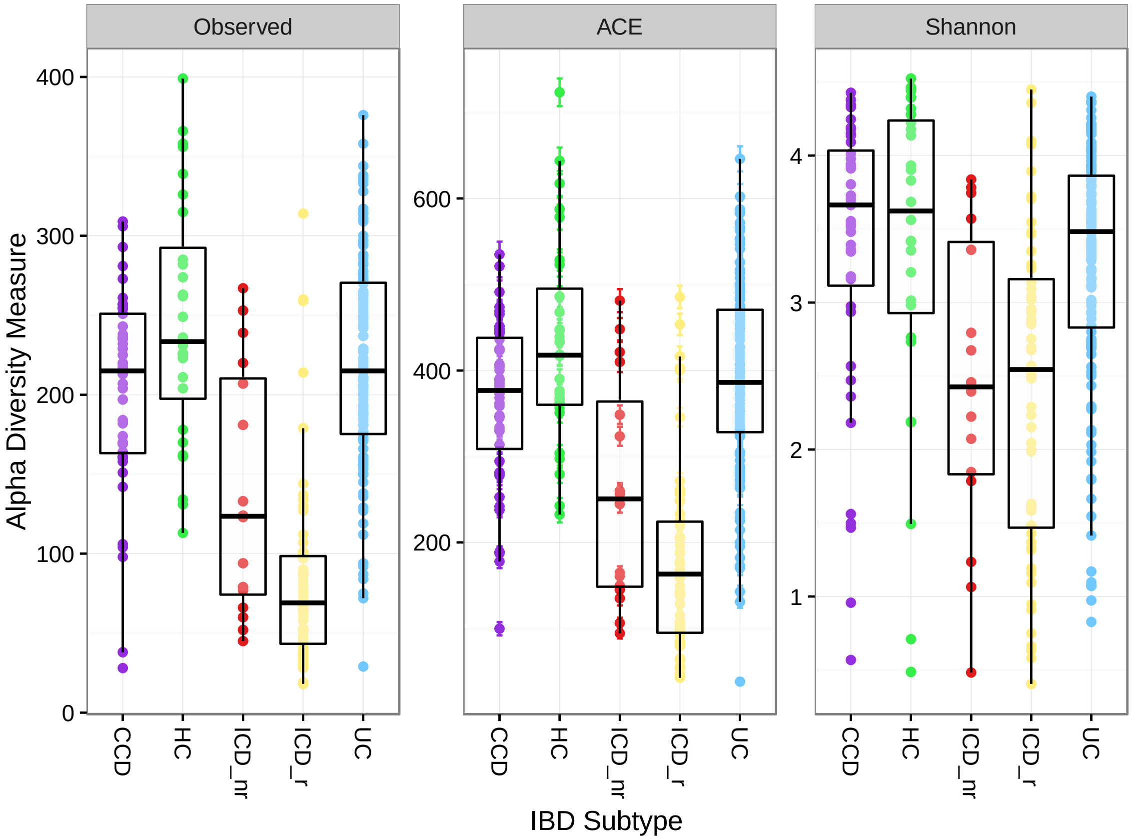
Fold-Change in Means	Proportion of OTUS with >80% Power	Median Power
1.25	0.9471	0.8432
1.5	0.9613	0.9015
2	1.0000	0.9999

The proportion of the 1000 OTUs which had at least 80% power and the median power over the 1000 OTUs for each fold change.

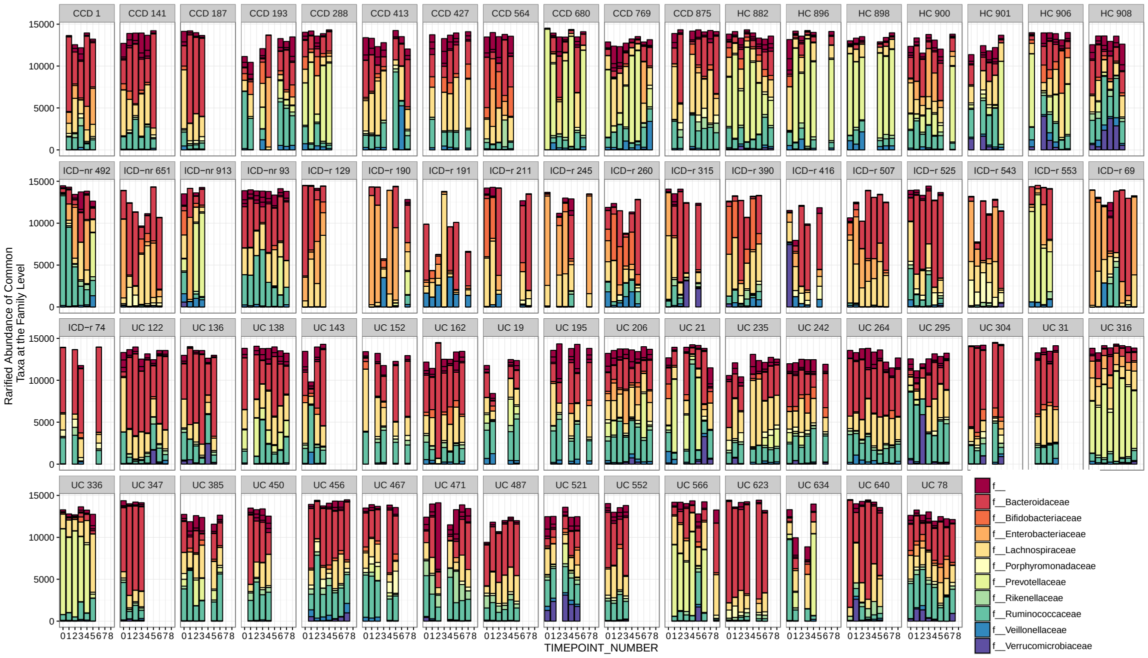
Supplementary Figure 1. The gut microbiomes of different IBD subtypes differ in community composition



Supplementary Figure 2. Alpha diversity of IBD-subtypes and healthy controls



Supplementary Figure 3. Microbiome dynamics of all individuals used in downstream analysis



Supplementary Figure 4. Shifts in microbiome structure in IBD patients with unstable medications