Supplementary Appendix

Methods

Study design

Patient inclusion criteria:

1. *C. difficile infection* was defined as diarrhea (⩾3 soft, loose or watery stools per day for at least 2 consecutive days or ⩾8 soft or loose stools in 48 hours) and a positive stool test for *C. difficile* toxin; and
2. Age ⩾ 18; and
3. Written informed consent obtained

Patient exclusion criteria:

1. The presence of human immunodeficiency virus (HIV) infection with a CD4 count of less than 240
2. Pregnancy
3. GI Bleeding
4. Acute coronary syndrome

Donor screening:

Donors included individuals who are spouses or partners, first-degree relatives, other relatives, friends, and individuals unknown to the patient. They were screened with a questionnaire and excluded if they had taken antibiotics within the preceding 3 months; were on major immunosuppressive agents, including chemotherapeutic agents; had known or recent exposure to HIV, hepatitis B or C; had a current communicable disease; participated in high-risk sexual behaviors; used illicit drugs; traveled within 6 months to areas with endemic diarrheal illnesses; or had history of inflammatory bowel disease, irritable bowel syndrome or chronic diarrhea, gastrointestinal malignancy or polyposis. In addition, donor was screened for HBsurface Ag, Anti-HBc, Anti-HCV, Anti-HIV, Syphilis EIA, stool microscopy, culture and sensitivity, stool cyst, ova, parasite, norovirus and *C. difficile* (cytotoxin and PCR assay). All subjects and collected stool samples are listed in **Supplementary Table 1**.

The donors for the FMT group were healthy household controls and the donor stool samples analyzed were the same samples used for FMT. All subjects provided written informed consent. The study was approved by The Joint Chinese University of Hong Kong, New Territories East Cluster Clinical Research Ethics Committee (The Joint CUHK-NTEC CREC, CREC Ref. No.: 2014.183-T; Clinical Trial registry, NCT02570477).

Family members provided donor stool for subjects randomised to FMT arm. Cure after FMT or vancomycin therapy was defined as symptom resolution and negative *Clostridium difficile* toxin in stool at last follow-up by PCR assay. Relapse was defined as diarrhea with a positive stool test for *C. difficile* toxin.

There is no pre-specified effective sample size for virome analysis. However, studies with as minimum as 4 twin pairs [1, 2] were able to define longitudinal changes in virome, therefore for this study nine subjects in the FMT arm and five in the standard antibiotic treatment (vancomycin) group respectively were expected to be sufficient.

This was a randomised but not blinded study. However for virome and bacterial microbiome analyses on stool samples, metagenomic assessments were initially performed by analysts who were blinded to the clinical outcome of the studied subjects. When the profiled virome and bacterial microbiome data were available for each individual subject, correlation was then made to associate microbiome profiles with treatment outcomes of subjects.

Infusion of donor stool

In subjects who received FMT, a nasoduodenal tube was inserted with radiology guidance. Donor feces was diluted with 500 ml of sterile saline (0.9%), blended and the supernatant was strained with filter paper and poured in a sterile bottle. Within 6 hours after collection of feces by the donor, the solution was infused through a nasoduodenal tube (2 to 3 minutes per 50 ml). The tube was removed 30 minutes after the infusion, and patients were monitored for 2 hours. In subjects with received FMT, a minimum of 50g of donor stool was collected on the same day of infusion and used within 6 hours of collection.

Subjects with norovirus infection and fecal viral metagenomic sequence data

17 patients with acute infectious diarrhea from confirmed norovirus infection (NI) [Median age, 69 years, IQR, 42-83) and a similar number of age-and gender-matched healthy controls were included. Stool samples were collected for Virus-like Particles (VLPs) enrichment and metagenomic sequencing. All subjects provided written informed consent. The study was approved by The Joint Chinese University of Hong Kong, New Territories East Cluster Clinical Research Ethics Committee (The Joint CUHK-NTEC CREC, CREC Ref. No.: CREC-2016.445).

Virus-like Particles (VLPs) enrichment

Approximately 200 mg of stool was suspended in 400μl saline-magnesium buffer (0.1 M NaCl, 0.008 M $MgSO_4 \cdot 7H_2O$, 0.002% gelatin, 0.05 M Tris pH7.5) by vortexing for 10 min. Stool suspensions were then cleared by centrifugation at 2,000 x g to remove debris and cells. Clarified suspensions were passed through one 0.45 mm followed by two 0.22 mm filters to remove residual host and bacterial cells. Samples were treated with lysozyme (1 mg/ml at 37 ℃ for 30 min) followed by chloroform (0.2x volume at RT for 10 min) to degrade any remaining bacterial and host cell membranes. Non-virus protected DNA was degraded by treatment with a DNase cocktail (10U Tubro DNaseI (Ambion), 1U Baseline zero DNase (Epicenter)) followed by heat inactivation of DNases at 65 ℃ for 10 min. VLPs were lysed (4% SDS plus 38 mg/ml Proteinase K at 56 ℃ for 20 min), treated with CTAB (2.5% CTAB plus 0.5 M NaCl at 65℃ for 10 min), and nucleic acid was extracted with phenol:chloroform pH 8.0 (Invitrogen). The aqueous fraction was washed once with an equal volume of chloroform, purified and concentrated on a column (DNA Clean & Concentrator^{TM}-5, Zymo Research). VLP DNA was amplified for 2 hr using Phi29 polymerase (GenomiPhi V2 kit, GE Healthcare) prior to sequencing. To reduce amplification bias, four independent reactions were performed for each sample and pooled together afterwards.

Sequence Processing and Quality Control

Raw reads were filtered by SOAPnuke (v 1.5.3) (http://soap.genomics.org.cn/) developed by BGI as follows: (i) adaptors removed, (ii) read removed if N base is more than 3% of the read, (iii) read removed if bases with quality low than 20 were more than 40% of read, (iv) all duplicates removed. Human sequences were removed from the quality-trimmed dataset by DeconSeq (v 0.4.3) with default parameters and the human reference GRCh38 [4].

De Novo Contig Assembly and Taxonomy Annotation

Contigs were assembled using the IDBA (v 1.1.1) [5], using maximum kmer length 120, with a minimum contig length of 1,000 bp. The assembled contigs were clustered at a 95% identity level using CD-HIT [6] to generate a unique contig consortium. Open Reading Frame (ORF) were predicted and extracted from contigs using the Glimmer3 toolkit (v 3.02) [7] and a minimum length threshold of 100 amino acids. The translated amino acid sequences of predicted ORFs from the VLP contigs were matched against the standard subset of the standalone entire UniProt TrEMBL database as of June 5, 2016, that contained only virus and phage reference proteins, using blastx (e<10-5) as described previously [8]. Each contig was assigned taxonomy based on the most abundant taxa contained within that contig using a voting system as described previously for virus taxonomic assignment at different taxon levels [9, 10]. The voting system first annotated each ORF of a contig of interest with the best-hit virus taxonomy. It then compared all of the taxonomic assignments of the ORFs within the contig of interest, and annotated the contig with the majority ORF assignment. Contigs with less than one ORF per 10kb were not assigned taxonomy as this suggests a contig of only limited similarity [9]. Contigs without a majority ORF taxonomic assignment due to ties of multiple major taxa were assigned as having multiple possible taxonomic annotations. Because some contigs shared the same taxonomic identities, the contig table was collapsed by taxonomic identity, meaning the contig relative abundances were summed if they shared identity. Taxa with relative abundance under 0.01% were disregarded for the purpose of further analyses. Richness and diversity calculation were performed using the estimate_richness function of the phyloseq package and plotted in GraphPad Prism (v 6.0) at the species and contig levels.

LEfSe linear discriminant analysis and Multivariate analysis

To compare differences in the configurations of virome and bacterial microbiome between CDI patients and healthy household controls, between FMT responders and non-responders, between FMT responders and vancomycin responders, Lefse analyses were performed on the Huttenhower lab Galaxy server (http://huttenhower.sph.harvard.edu/galaxy/) by importing the viral and bacterial relative abundance values and associated sample metadata, with FDR adjusted p value<0.05 considered significant and effect size calculated. MaAsLin (Multivariate Analysis by Linear Models) was implemented to identify associations between clinical metadata (age, sex, family ID, time samples were collected) and viral community abundance matrix on the Huttenhower lab Galaxy server (http://huttenhower.sph.harvard.edu/galaxy/).

Stool Bacterial DNA Extraction

Stool bacterial DNA was extracted from aliquots of human stool sample using ZR Fecal DNA miniPrep kit (Zymo Research, Orange, CA) according to the protocal. Briefly, 150 mg of fecal sample was added to the BashingBeadLysis Tube with 750 μl Lysis solution, and then processed at maximum speed for ⩾ 5 minutes. The lysates were centrifugeed at ⩾ 10,000 x g for 1 minute. The supernatant was transferred to a Zymo-Spin^{TM} IV Spin Filter in a collection tube and centrifuged at 7,000 x g for 1 minute. About 1,200 μl of fecal DNA binding buffer was added to the filtrate in the collection tube, followed by concentration and purification in a new filter tube. Finally, a total of 50 μl eluted DNA with a concentration at 20-100 ng/μl was prepared for each sample.

16S rRNA sequencing and quality control

The final fecal DNA samples were sequenced on the Illumina MiSeq platform (V4 region, 2 X 250 bp), 112,482 ± 66,095 (number ± SD) sequences obtained on average (sequence statistics in **Supplementary Table 3**). Quality control and data analysis were implemented in mothur (v 1.38.0) as previously described [11]. Any sequences with ambiguous bases and anything longer than 275 bp were removed, and aligned against the non-redundant Greengenes database (v 13.8) [12] using the NAST algorithm. Any sequences that failed to align with the V3-4 region were discarded. The remaining sequences were trimmed to the same alignment coordinates over which they fully overlapped, followed by removal of homopolymers and detection for the presence of chimeras by UChime.

16S rRNA sequencing data analysis

The resulting sequences were classified against the Greengenes database and annotated with deepest level taxa represented by pseudo-bootstrap confidence scores of at least 80% averaged over 1,000 iterations of the naive Bayesian classifier. Any sequences that were classified as either being originated from archaea, eukarya, chloroplasts, mitochondria, or unknown kingdoms, were removed. The annotated sequences were assigned to phylotypes according to their consensus taxonomy with which at least 80% of the sequences agreed. Closed reference operational taxonomic units (OTUs) sharing 97% identity were clustered as well and assigned taxonomy according to the Greengenes database. Lefse analysis was performed to define bacterial taxa associated with CDI and healthy controls. The relative abundance of these abundance-differential taxa identified by Lefse in pre-FMT baseline samples and post-FMT last follow-up samples were plotted using *pheatmap* R package.

Results

Supplementary Table 1 Summary of study subjects and samples

sample#	sample_NAME	Sample_collection	time_point_post_FMT (week)	time_point_post_standard_therapy (week)	baseline_comparasion	FMT_number	LABEL	Time of sample collection	Household(famiy_ID)	Age	Sex
1	C1W0	cross-sectional	NA	NA	CDI	NA	A0198ST1	19-Jan-15	A	86	F
2	N1W0	cross-sectional	NA	NA	Control	NA	A0222ST1	04-Mar-15	A		
3	C2W0	cross-sectional	NA	NA	CDI	NA	A0393ST2	26-Nov-15	C		
4	N2W0	cross-sectional	NA	NA	Control	NA	A0417ST1	11-Dec-15	C		
5	C3W0	cross-sectional	NA	NA	CDI	NA	A0300ST1	24-Jul-15	J	80	F
6	N3W0	cross-sectional	NA	NA	Control	NA	A0297ST1	21-Jul-15	J	55	F
7	C4W0	cross-sectional	NA	NA	CDI	NA	A0345ST1	31-Aug-15	M	66	F
8	N4W0	cross-sectional	NA	NA	Control	NA	A0339ST1	26-Aug-15	M	41	M
9	F10W0	longitudinal	NA	NA	CDI	NA	A0347ST1	07-Sep-15	O	84	M
10	D10W0	cross-sectional	NA	NA	Control	NA	A0348ST1	08-Sep-15	O	42	M
11	C6W0	cross-sectional	NA	NA	CDI	NA	A0374ST1	08-Oct-15	S	76	M
12	C5W0	cross-sectional	NA	NA	CDI	NA	A0419ST1	11-Dec-15	U	25	F
13	N5W0	cross-sectional	NA	NA	Control	NA	A0424ST1	24-Dec-15	U	33	M
14	N6W0	cross-sectional	NA	NA	Control	NA	A0407ST1	26-Jan-16	V	45	F
15	N7W0	cross-sectional	NA	NA	Control	NA	A0189ST1	23-Dec-15	W	56	F
16	N8W0	cross-sectional	NA	NA	Control	NA	A0436ST1	08-Jan-16	X	36	F
17	N9W0	cross-sectional	NA	NA	Control	NA	A00448ST1	22-Jan-16	Y	43	F
18	N10W0	cross-sectional	NA	NA	Control	NA	A0454ST1	27-Jan-16	Z	85	F
19	C7W0	cross-sectional	NA	NA	CDI	NA	A0435ST1	07-Jan-16	AA	81	M
20	C8W0	cross-sectional	NA	NA	CDI	NA	A0438ST1	15-Jan-16	Y	99	M
21	C9W0	cross-sectional	NA	NA	CDI	NA	A0445ST1	21-Jan-16	Z		
22	N11W0	cross-sectional	NA	NA	Control	NA	A0408ST1	26-Jan-16	AB	45	F
23	F1W0	longitudinal	0	NA	CDI	FMT1	A0394ST1	27-Oct-15	B		

24	F1W2	longitudinal	2	NA	NA	FMT1	A0394ST2	16-Nov-15	B		
25	F1W6	longitudinal	6	NA	NA	FMT1	A0394ST3	14-Dec-15	B		
26	D1W0	cross-sectional	0	NA	Control	Donor 1	A0392ST1	27-Oct-15	B		
27	F2W0	longitudinal	0	NA	CDI	FMT2	A0214ST1	13-Feb-15	D	52	M
28	F2W2	longitudinal	2	NA	NA	FMT2	A0214ST2	06-Mar-15	D	52	M
29	F2W4	longitudinal	4	NA	NA	FMT2	A0214ST5	20-Mar-15	D	52	M
30	F2W27	longitudinal	27	NA	NA	FMT2	A0214ST7	28-Aug-15	D	52	M
31	D2W0	cross-sectional	0	NA	Control	Donor 2	A0213ST1	12-Feb-15	D	51	F
32	F3W0	longitudinal	0	NA	CDI	FMT3	A0228ST1	20-Mar-15	F	38	M
33	F3W2	longitudinal	2	NA	NA	FMT3	A0228ST2	14-Apr-15	F	38	M
34	F3W4	longitudinal	4	NA	NA	FMT3	A0228ST3	28-Apr-15	F	38	M
35	F3W10	longitudinal	10	NA	NA	FMT3	A0228ST4	02-Jun-15	F	38	M
36	F3W17	longitudinal	17	NA	NA	FMT3	A0228ST6	28-Jul-15	F	38	M
37	D3W0	cross-sectional	0	NA	Control	Donor 3	A0229ST1	20-Mar-15	F	73	M
38	F4W0	longitudinal	0	NA	CDI	FMT4	A0271ST1	03-Jun-15	H	76	F
39	F4W2	longitudinal	2	NA	NA	FMT4	A0271ST2	29-Jun-15	H	76	F
40	F4W4	longitudinal	4	NA	NA	FMT4	A0271ST3	06-Jul-15	H	76	F
41	F4W5	longitudinal	5	NA	NA	FMT4	A0271ST4	13-Jul-15	H	76	F
42	F4W10	longitudinal	10	NA	NA	FMT4	A0271ST6	20-Aug-15	H	76	F
43	F4W18	longitudinal	18	NA	NA	FMT4	A0271ST7	16-Oct-15	H	76	F
44	D4W0	cross-sectional	0	NA	Control	Donor 4	A0265ST1	01-Jun-15	H	53	F
45	F5W0	longitudinal	0	NA	CDI	FMT5	A0310ST1	30-Jul-15	K	63	M
46	F5W2	longitudinal	2	NA	NA	FMT5	A0310ST2	18-Aug-15	K	63	M
47	F5W10	longitudinal	10	NA	NA	FMT5	A0310ST3	19-Oct-15	K	63	M
48	F5W18	longitudinal	18	NA	NA	FMT5	A0310ST4	14-Dec-15	K	63	M
49	D5W0	cross-sectional	0	NA	Control	Donor 5	A0313ST1	31-Jul-15	K	36	F

50	F6W0	longitudinal	0	NA	CDI	FMT6	A0326ST1	21-Aug-15	L	88	M
51	F6W2	longitudinal	2	NA	NA	FMT6	A0326ST2	17-Sep-15	L	88	M
52	F6W4	longitudinal	4	NA	NA	FMT6	A0326ST3	01-Oct-15	L	88	M
53	F6W11	longitudinal	11	NA	NA	FMT6	A0326ST4	20-Nov-15	L	88	M
54	D6W0	cross-sectional	0	NA	Control	Donor 6	A0336ST1	24-Aug-15	L	41	M
55	F7W0	longitudinal	0	NA	CDI	FMT7	A0340ST1	26-Aug-15	N	45	M
56	F7W2	longitudinal	2	NA	NA	FMT7	A0340ST2	22-Sep-15	N	45	M
57	F7W6	longitudinal	6	NA	NA	FMT7	A0340ST3	22-Oct-15	N	45	M
58	F7W10	longitudinal	10	NA	NA	FMT7	A0340ST4	18-Nov-15	N	45	M
59	D7W0	cross-sectional	0	NA	Control	Donor 7	A0346ST1	02-Sep-15	N	21	M
60	F8W0	longitudinal	0	NA	CDI	FMT8	A0373ST1	30-Sep-15	Q	83	F
61	F8W2	longitudinal	2	NA	NA	FMT8	A0373ST2	18-Oct-15	Q	83	F
62	F8W4	longitudinal	4	NA	NA	FMT8	A0373ST3	04-Nov-15	Q	83	F
63	D8W0	cross-sectional	0	NA	Control	Donor 8	A0370ST1	25-Sep-15	Q	57	M
64	F9W0	longitudinal	0	NA	CDI	FMT9	A0371ST1	24-Sep-15	R	38	F
65	F9W2	longitudinal	2	NA	NA	FMT9	A0371ST2	19-Oct-15	R	38	F
66	F9W4	longitudinal	4	NA	NA	FMT9	A0371ST3	05-Nov-15	R	38	F
67	F9W10	longitudinal	10	NA	NA	FMT9	A0371ST4	28-Dec-15	R	38	F
68	S1W0	longitudinal	NA	0	CDI	ST1	A0223ST1	06-Mar-15	E	88	M
69	S1W2	longitudinal	NA	2	NA	ST1	A0223ST2	18-Mar-15	E	88	M
70	S1W5	longitudinal	NA	5	NA	ST1	A0223ST3	11-Apr-15	E	88	M
71	S1W10	longitudinal	NA	10	NA	ST1	A0223ST4	05-May-15	E	88	M
72	S2W0	longitudinal	NA	0	CDI	ST2	A0256ST1	07-May-15	G	93	M
73	S2W2	longitudinal	NA	2	NA	ST2	A0256ST2	22-May-15	G	94	M
74	S3W0	longitudinal	NA	0	CDI	ST3	A0293ST1	14-Jul-15	I	78	F
75	S3W2	longitudinal	NA	2	NA	ST3	A0293ST2	24-Jul-15	I	78	F
76	S3W4	longitudinal	NA	4	NA	ST3	A0293ST3	10-Aug-15	I	78	F

77	S4W0	longitudinal	NA	0	CDI	ST4	A0369ST1	24-Sep-15	P	83	F
78	S4W2	longitudinal	NA	2	NA	ST4	A0369ST2	05-Oct-15	P	84	F
79	S4W4	longitudinal	NA	4	NA	ST4	A0369ST3	19-Oct-15	P	85	F
80	S4W10	longitudinal	NA	10	NA	ST4	A0369ST4	30-Nov-15	P	86	F
81	S5W0	longitudinal	NA	0	CDI	ST5	A0376ST1	20-Oct-15	T	99	F
82	S5W2	longitudinal	NA	2	NA	ST5	A0376ST2	02-Nov-15	T	99	F
83	S5W4	longitudinal	NA	4	NA	ST5	A0376ST3	16-Nov-15	T	99	F

Supplementary Table 2. Read Statistics for VLPs metagenomic sequencing data

sample_number	**stratege**	**Clean Reads (with duplicates)**	**Raw Data(bp)**	**Clean Data(bp)**	**Clean Data/Raw Data(%)**	**Q20(%)**	**Insert Size**	**Read Length(bp)**	**Clean Reads (deduplicates)**	**Clean Data(bp)**	**dehuman contamination clean reads**
C1W0	PE	62775238	9991197000	9416285700	94.25	97.68	270	150	35310274	5296541100	35259895
N1W0	PE	61051824	9771340800	9157773600	93.72	97.66	270	150	35174258	5276138700	35138622
F1W0	PE	72908524	11628734400	10936278600	94.05	97.73	270	150	49258666	7388799900	49214972
F1W2	PE	61452336	9879645900	9217850400	93.30	97.64	270	150	37950160	5692524000	37877002
F1W6	PE	61937734	9901291200	9290660100	93.83	97.47	270	150	36773522	5516028300	36694663
D1W0	PE	71971260	11632557300	10795689000	92.81	97.56	270	150	60530028	9079504200	60156905
C2W0	PE	54404614	8603408400	8160692100	94.85	97.78	270	150	30454726	4568208900	30429234
N2W0	PE	58876302	9679518000	8831445300	91.24	96.99	270	150	47090320	7063548000	46270650
F2W0	PE	63222294	9483344100	9483344100	93.22	97.24	270	150	47609728	7141459200	47383851
F2W2	PE	57069572	9181378500	8560435800	93.24	97.44	270	150	26486692	3973003800	26460992
F2W4	PE	56474014	9258392400	8471102100	91.50	97.35	270	150	31534626	4730193900	31385993
F2W27	PE	62855360	9951258600	9428304000	94.74	97.58	270	150	40976008	6146401200	40920048
D2W0	PE	65188562	10492993800	9778284300	93.19	97.50	270	150	47035814	7055372100	46771547

S1W0	PE	78560738	12704849100	11784110700	92.75	96.61	270	150	69986282	10497942300	61254628
F3W0	PE	63633346	10132440000	9545001900	94.20	97.70	270	150	44325384	6648807600	44226661
F3W2	PE	67863116	11041764600	10179467400	92.19	97.17	270	150	55736426	8360463900	55003416
F3W4	PE	54546192	8841385200	8181928800	92.54	97.62	270	150	19938070	2990710500	19912084
F3W10	PE	56402642	9026390400	8460396300	93.73	97.51	270	150	32904412	4935661800	32858523
F3W17	PE	57655702	9308481600	8648355300	92.91	97.28	270	150	51164390	7674658500	50799218
D3W0	PE	60398538	9677539500	9059780700	93.62	97.57	270	150	43593004	6538950600	43551379
S2W0	PE	62029898	9921949800	9304484700	93.78	97.22	270	150	19587122	2938068300	19481164
F4W0	PE	70249768	11417761500	10537465200	92.29	97.19	270	150	58701008	8805151200	53599900
F4W2	PE	72291124	11593675200	10843668600	93.53	97.28	270	150	42625764	6393864600	42189098
F4W4	PE	55309580	9022624200	8296437000	92.78	97.05	270	150	22071026	3310653900	21947324
F4W5	PE	56341336	9447712200	8451200400	89.45	96.52	270	150	37547642	5632146300	34620382
F4W10	PE	67820766	10802030400	10173114900	94.18	97.26	270	150	50790294	7618544100	49718303
F4W18	PE	62542160	10187530200	9381324000	92.91	97.21	270	150	52058076	7808711400	51790343
D4W0	PE	65414574	10647087300	9812186100	92.98	97.22	270	150	45517454	6827618100	45407834
S3W0	PE	49856060	8095937400	7478409000	93.20	97.34	270	150	27871988	4180798200	27649327
C3W0	PE	52795414	8536192800	7919312100	93.60	97.61	270	150	19745338	2961800700	19717506
N3W0	PE	67781664	10971849600	10167249600	92.67	96.97	270	150	48616360	7292454000	44963381
F5W0	PE	59464284	9818251800	8919642600	91.67	96.84	270	150	53191940	7978791000	50866340
F5W2	PE	58990474	9742672200	8848571100	91.64	96.78	270	150	52190752	7828612800	51029410
F5W10	PE	70767788	11524117200	10615168200	92.94	97.47	270	150	48194014	7229102100	48131665
F5W18	PE	56344752	9110928000	8451712800	92.76	97.39	270	150	48746752	7312012800	45555999
D5W0	PE	56276446	9212273400	8441466900	92.45	97.21	270	150	49072324	7360848600	48408340
F6W0	PE	66880946	10848952800	10032141900	92.47	97.62	270	150	33865442	5079816300	33828462
F6W2	PE	49343280	8023825500	7401492000	93.08	97.27	270	150	34613026	5191953900	34531700
F6W4	PE	68396004	11080149600	10259400600	92.59	97.62	270	150	50626182	7593927300	50483872
F6W11	PE	59587740	9505559700	8938161000	94.03	97.56	270	150	40184974	6027746100	39896849

D6W0	PE	71249914	11956911900	10687487100	89.38	96.18	270	150	63489090	9523363500	54552750
C4W0	PE	64764190	10604839500	9714628500	92.42	96.93	270	150	56952558	8542883700	56071573
N4W0	PE	68626222	10919059800	10293933300	94.27	97.78	270	150	45536348	6830452200	45429927
F7W0	PE	60637808	10019179800	9095671200	90.78	96.77	270	150	52360482	7854072300	51171286
F7W2	PE	53007420	8590338300	7951113000	92.56	97.27	270	150	45056108	6758416200	44968493
F7W6	PE	60265864	9626333100	9039879600	93.91	97.88	270	150	28086594	4212989100	28056380
F7W10	PE	55566500	8885519700	8334975000	93.80	97.60	270	150	32341864	4851279600	30309892
D7W0	PE	63959224	10260963600	9593883600	93.50	97.43	270	150	55051970	8257795500	54945617
F8W0	PE	60709794	9837748800	9106469100	92.57	96.88	270	150	52220104	7833015600	50666863
F8W10	PE	67005004	10768592400	10050750600	93.33	97.41	270	150	56329118	8449367700	56065034
D8W0	PE	54733124	8822077200	8209968600	93.06	97.39	270	150	43918160	6587724000	43793944
S4W0	PE	52048562	8311757400	7807284300	93.93	97.48	270	150	39097068	5864560200	38954427
F8W0	PE	55373256	8896104000	8305988400	93.37	97.58	270	150	36786824	5518023600	36710287
F8W2	PE	52773494	8419165500	7916024100	94.02	97.62	270	150	26959886	4043982900	26919104
F8W4	PE	62692276	10020003000	9403841400	93.85	97.37	270	150	34653832	5198074800	34607286
D8W0	PE	54325118	8650715100	8148767700	94.20	97.68	270	150	15930846	2389626900	15911391
F9W0	PE	57743068	9351227700	8661460200	92.62	97.17	270	150	50944548	7641682200	50758607
F9W2	PE	62521482	10080941400	9378222300	93.03	97.51	270	150	54102762	8115414300	53911905
F9W4	PE	55870900	9226278600	8380635000	90.83	95.38	270	150	51415752	7712362800	51140562
F9W10	PE	55794488	9027887700	8369173200	92.70	97.11	270	150	48465562	7269834300	48322767
C6W0	PE	50764752	8176121400	7614712800	93.13	97.38	270	150	32306284	4845942600	32272121
S5W0	PE	59301276	9633133200	8895191400	92.34	97.12	270	150	51022936	7653440400	50655870
C5W0	PE	67889284	10923227100	10183392600	93.23	97.56	270	150	57358300	8603745000	56812376
N5W0	PE	59708564	9509021700	8956284600	94.19	97.63	270	150	24030544	3604581600	23970287
N6W0	PE	62723994	10067253900	9408599100	93.46	97.62	270	150	54089868	8113480200	53257937
N7W0	PE	59306006	9430123200	8895900900	94.33	97.58	270	150	45422294	6813344100	45222130
N8W0	PE	65684456	10506488100	9852668400	93.78	97.81	270	150	28838700	4325805000	28687505

N9W0	PE	63649198	10202578800	9547379700	93.58	97.39	270	150	41104988	6165748200	39227638
N10W0	PE	50235066	8120349600	7535259900	92.79	97.37	270	150	33913816	5087072400	33631989
C7W0	PE	66179220	10552657800	9926883000	94.07	97.45	270	150	43113060	6466959000	31933029
C8W0	PE	64891662	10394203500	9733749300	93.65	97.57	270	150	48024320	7203648000	47357742
C9W0	PE	58954002	9377404800	8843100300	94.30	97.37	270	150	43761166	6564174900	43535848
N11W0	PE	62169334	10005166200	9325400100	93.21	97.46	270	150	33477790	5021668500	32776670

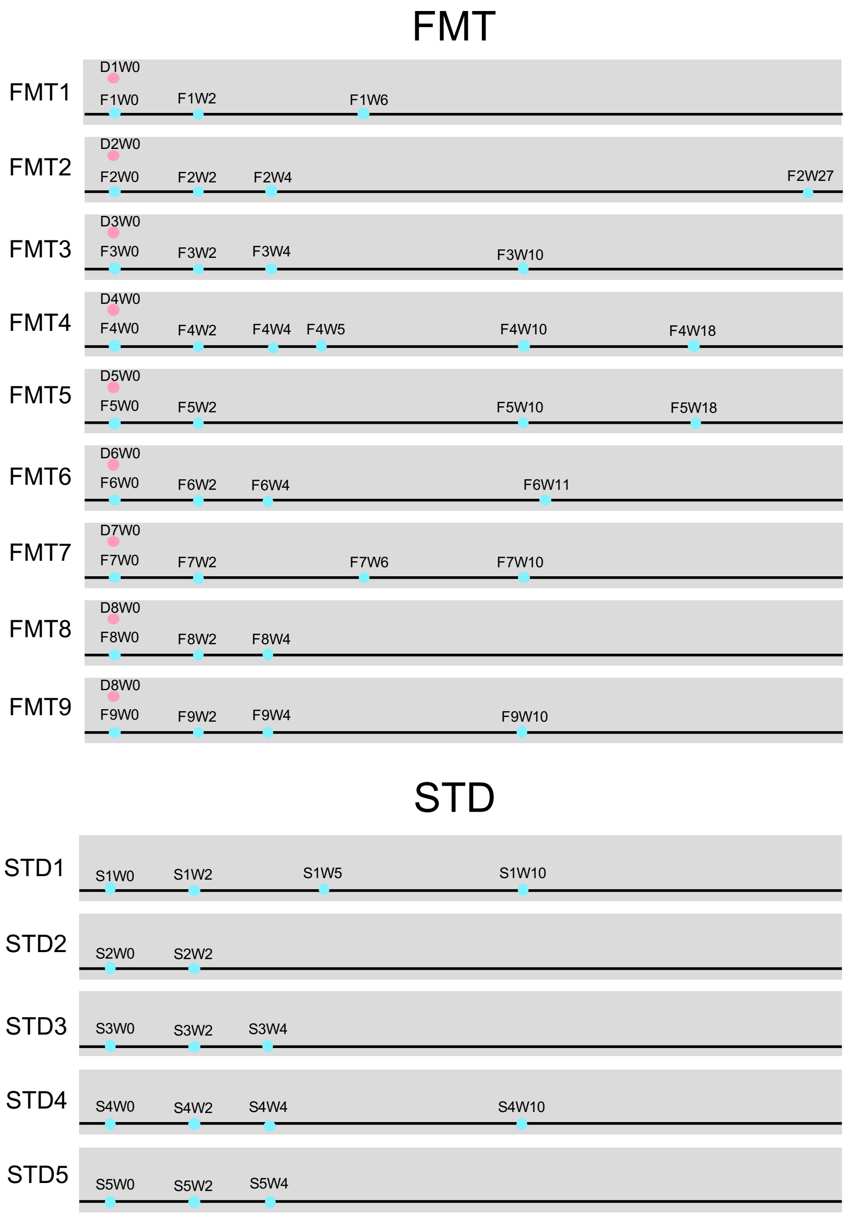
Supplementary Table 3. Read Statistics for 16S rRNA sequencing data

sample_number	length	raw_reads	raw_data(bp)	Raw_Q20	Raw_Q30	clean_data/raw_data	clean_reads	clean_data(bp)	Clean_Q20	Clean_Q30	GC_rate	GC(AT)_separation_rate
C1W0	250	93298	23324500	96.10;92.98	93.82;89.12	29.23	27272	6818000	90.95;86.26	85.95;79.43	54.54	18.93
N1W0	250	127534	31883500	96.30;90.93	94.05;85.88	52.3	66694	16673500	94.68;88.01	91.53;81.50	55.41	19.19
F1W0	250	139020	34755000	95.79;90.83	93.15;85.69	36.41	50614	12653500	91.85;85.01	87.02;76.95	54.77	17.07
F1W2	250	453216	113304000	95.27;90.75	92.40;85.70	49.63	224930	56232500	92.95;87.45	88.68;80.73	55.19	18.81
F1W6	250	210766	52691500	95.52;90.59	92.85;85.53	54.7	115298	28824500	93.84;88.21	90.17;81.93	54.43	18.58
D1W0	250	197162	49290500	95.44;90.44	92.62;85.30	56.09	110582	27645500	93.87;88.04	90.13;81.74	53.81	17.97
C2W0	250	115544	28886000	95.12;84.81	91.98;77.68	47.42	54786	13696500	93.25;86.61	89.04;79.19	55.67	18.71
N2W0	250	192726	48181500	95.22;86.64	92.12;80.11	49.58	95562	23890500	93.50;87.60	89.36;80.64	55.47	18.54
F2W0	250	145174	36293500	96.29;91.02	93.94;85.80	36.12	52432	13108000	92.64;84.95	88.18;76.72	56.19	17.67
F2W2	250	165058	41264500	94.71;92.06	91.46;87.64	39.87	65806	16451500	91.65;88.07	86.57;81.70	53.31	16.39
F2W4	250	157286	39321500	93.74;89.94	89.79;84.38	51.06	80306	20076500	92.01;87.03	86.90;79.90	55.57	17.8
F2W27	250	166280	41570000	92.96;89.93	88.53;84.40	54.03	89846	22461500	91.33;87.54	85.83;80.71	55.26	17.98
D2W0	250	178348	44587000	96.09;91.21	93.73;86.43	53.95	96226	24056500	94.52;88.60	91.28;82.59	53.59	17.7
S1W0	250	144110	36027500	95.66;89.74	92.89;84.18	50.6	72918	18229500	93.52;87.20	89.48;80.29	54.66	18

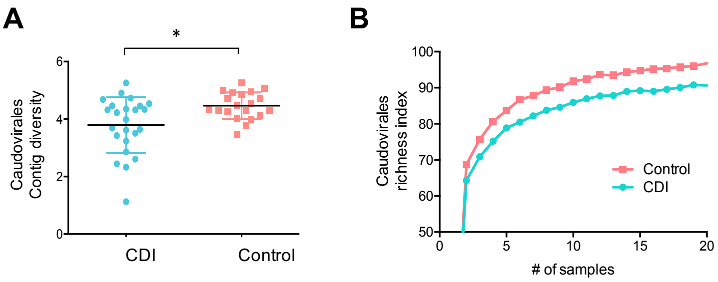
F3W0	250	392454	98113500	95.24;90.96	92.45;86.49	37.82	148440	37110000	91.53;86.47	86.87;79.95	51.66	17.84
F3W2	250	230982	57745500	94.93;91.76	91.83;87.24	44.39	102532	25633000	92.27;88.60	87.55;82.49	54.01	17.61
F3W4	250	112378	28094500	95.35;91.60	92.47;87.16	47.17	53006	13251500	93.19;88.74	88.96;82.86	53.36	18.24
F3W10	250	230772	57693000	95.05;91.29	92.05;86.79	44.67	103090	25772500	92.61;88.66	88.16;82.79	52.81	17.76
F3W17	250	311224	77806000	95.80;90.74	93.16;85.68	44.88	139674	34918500	93.46;86.87	89.48;79.89	54.17	17.5
D3W0	250	523854	130963500	95.96;91.67	93.55;87.14	48.24	252724	63181000	93.84;88.65	90.26;82.68	53.82	17.61
S2W0	250	141758	35439500	96.21;91.31	93.89;86.53	41.43	58734	14683500	93.30;86.56	89.34;79.61	54.25	17.83
F4W0	250	174036	43509000	94.98;91.93	91.98;87.39	41.06	71452	17863000	91.59;87.69	86.66;81.07	54.33	17.79
F4W2	250	220990	55247500	95.67;90.72	92.87;85.31	43.23	95524	23881000	92.80;86.49	88.26;78.96	55.18	17.57
F4W4	250	241624	60406000	96.06;92.31	93.65;87.95	36.16	87376	21844000	92.41;86.99	87.93;80.09	55.01	17.9
F4W5	250	180292	45073000	96.00;88.58	93.18;81.91	47.99	86526	21631500	93.76;84.66	89.47;75.90	58.15	18.24
F4W10	250	170844	42711000	95.79;89.19	93.05;83.09	45.49	77718	19429500	93.10;85.08	88.76;76.93	56.41	19.63
F4W18	250	201408	50352000	95.22;90.83	92.19;85.76	43.77	88154	22038500	91.86;87.35	86.86;80.61	54.42	17.76
D4W0	250	421468	105367000	95.48;91.52	92.80;86.95	49.82	209980	52495000	93.28;88.61	89.38;82.63	53.83	18.38
S3W0	250	127724	31931000	95.51;90.51	92.80;85.42	48.49	61934	15483500	93.12;87.26	89.11;80.65	53.3	18.06
C3W0	250	186468	46617000	95.95;91.35	93.48;86.45	39.94	74474	18618500	92.77;86.52	88.54;79.29	54.38	18.5
N3W0	250	253674	63418500	95.90;90.49	93.47;85.75	46.68	118412	29603000	93.54;86.99	89.85;80.72	51.69	17.47
F5W0	250	141266	35316500	95.72;92.24	93.29;88.04	37.14	52462	13115500	92.29;87.48	88.03;81.02	53.82	17.02
F5W2	250	144132	36033000	95.57;92.50	93.00;88.62	32.13	46310	11577500	90.82;86.17	86.05;79.34	53.24	17.31
F5W10	250	218376	54594000	95.84;90.61	93.41;85.54	38.59	84272	21068000	92.46;85.13	88.15;77.47	54.1	17.83
F5W18	250	238492	59623000	95.60;91.57	92.89;86.95	36.26	86488	21622000	91.76;85.94	86.79;78.68	53.76	17.52
D5W0	250	350844	87711000	95.91;91.00	93.44;86.18	46.31	162472	40618000	93.40;87.15	89.56;80.42	54.36	18.42
F6W0	250	266526	66631500	95.02;92.91	92.15;88.81	37.13	98972	24743000	90.92;88.31	85.86;81.84	54.74	16.86
F6W2	250	236454	59113500	94.97;87.97	91.90;81.96	44.09	104262	26065500	92.28;86.86	87.71;79.83	53.8	17.56
F6W4	250	147466	36866500	95.57;91.03	92.91;86.19	45.42	66978	16744500	93.05;87.85	89.03;81.39	53.98	17.64
F6W11	250	233562	58390500	94.26;91.59	90.82;86.97	45.15	105462	26365500	90.98;88.26	85.76;81.91	54.06	17.48
D6W0	250	305446	76361500	95.58;90.07	92.80;84.61	55.31	168944	42236000	93.98;87.48	90.22;80.72	54.78	18.24

C4W0	250	168938	42234500	93.48;91.86	89.78;87.13	32.75	55330	13832500	87.80;86.11	81.01;78.38	54.64	16.78
N4W0	250	356614	89153500	95.81;91.21	93.14;86.30	48.47	172844	43211000	93.53;87.82	89.57;81.25	54.23	17.68
F7W0	250	283910	70977500	95.39;91.97	92.67;87.39	33.77	95884	23971000	90.79;85.86	85.54;78.32	55.08	18.15
F7W2	250	200238	50059500	96.30;92.38	94.04;87.90	30.26	60588	15147000	91.65;85.35	86.84;77.46	55.17	18.01
F7W6	250	170482	42620500	94.67;92.70	91.49;88.64	38.49	65614	16403500	90.65;88.04	85.26;81.81	54.36	17.75
F7W10	250	178994	44748500	93.84;91.64	90.14;86.78	36.65	65606	16401500	88.94;86.33	82.46;78.70	54.59	17.54
D7W0	250	824186	206046500	95.85;92.62	93.41;88.60	40.69	335336	83834000	92.78;88.86	88.76;83.02	53.36	18.13
F8W0	250	144894	36223500	96.49;92.85	94.43;88.97	27.61	39998	9999500	91.41;85.43	86.62;78.33	54.42	19.12
F8W10	250	286358	71589500	95.20;90.58	92.03;85.16	49.98	143108	35777000	92.84;87.39	88.32;80.44	55.52	18.48
D8W0	250	474850	118712500	94.68;90.59	91.42;85.26	50.34	239062	59765500	92.14;87.42	87.45;80.50	55.47	18.24
S4W0	250	223636	55909000	95.97;91.96	93.32;87.20	31.94	71434	17858500	91.21;85.22	85.78;76.95	55.8	17.11
F8W0	250	215272	53818000	94.62;91.02	91.31;86.15	42.74	92012	23003000	91.26;86.45	86.01;79.52	53.28	16.25
F8W2	250	195352	48838000	95.40;91.19	92.63;86.51	44.86	87634	21908500	92.55;87.56	88.23;81.09	53.31	16.97
F8W4	250	193674	48418500	95.84;92.93	93.36;88.86	29.48	57096	14274000	90.62;86.02	85.33;78.64	55.18	18.32
D8W0	250	183434	45858500	93.90;91.76	90.07;86.93	47.41	86968	21742000	91.60;88.79	86.38;82.41	55.82	18.57
F9W0	250	130132	32533000	96.33;91.93	94.23;87.95	28.16	36646	9161500	90.94;83.79	86.02;76.52	51.56	18.11
F9W2	250	256932	64233000	94.64;91.89	91.56;87.57	47.87	122998	30749500	92.27;88.76	87.79;82.99	52.79	17.91
F9W4	250	442748	110687000	95.87;91.18	93.38;86.58	38.11	168732	42183000	92.35;85.88	87.97;78.81	52.41	17.55
F9W10	250	376794	94198500	95.75;90.40	93.04;85.16	44.61	168084	42021000	93.07;86.18	88.81;78.89	54.27	18.06
C6W0	250	225218	56304500	95.78;93.02	93.16;88.78	28.02	63114	15778500	90.04;85.79	84.32;77.77	55.92	16.95
S5W0	250	241924	60481000	95.83;92.35	93.20;87.91	32.86	79506	19876500	91.30;86.11	86.02;78.66	55.38	17.27
C5W0	250	232140	58035000	95.60;90.53	92.72;84.82	36.89	85644	21411000	91.50;84.58	86.25;75.83	56.9	18.42
N5W0	250	279832	69958000	95.29;91.46	92.52;86.79	57.13	159864	39966000	93.75;89.41	90.13;83.74	54.04	18.52
N6W0	250	588188	147047000	95.50;92.07	92.83;87.77	49.31	290050	72512500	93.22;89.13	89.38;83.50	52.71	17.14
N7W0	250	510334	127583500	95.87;91.61	93.37;87.05	50.07	255508	63877000	93.89;88.61	90.30;82.63	53.17	17.37
N8W0	250	203468	50867000	93.42;91.18	89.27;86.35	50.32	102382	25595500	91.35;88.52	85.82;82.31	54.61	18.35

N9W0	250	242486	60621500	94.36;91.01	90.81;85.96	58.72	142396	35599000	92.93;89.03	88.49;82.94	55.31	18.25
N10W0	250	462154	115538500	95.48;92.10	92.79;87.83	48.56	224408	56102000	93.08;89.09	89.09;83.40	53.21	17.69
C7W0	250	192778	48194500	96.05;89.98	93.84;84.79	45.56	87836	21959000	93.72;86.32	90.25;79.32	53.87	18.89
C8W0	250	295522	73880500	96.32;92.60	94.16;88.49	35.97	106314	26578500	92.80;87.26	88.75;80.63	54.32	18.36
C9W0	250	131878	32969500	96.16;92.69	93.89;88.70	26.67	35168	8792000	90.64;84.74	85.32;77.30	54.94	19.39
N11W0	250	519884	129971000	95.94;90.60	93.51;85.62	52.17	271218	67804500	94.25;87.82	90.90;81.51	52.91	17.3

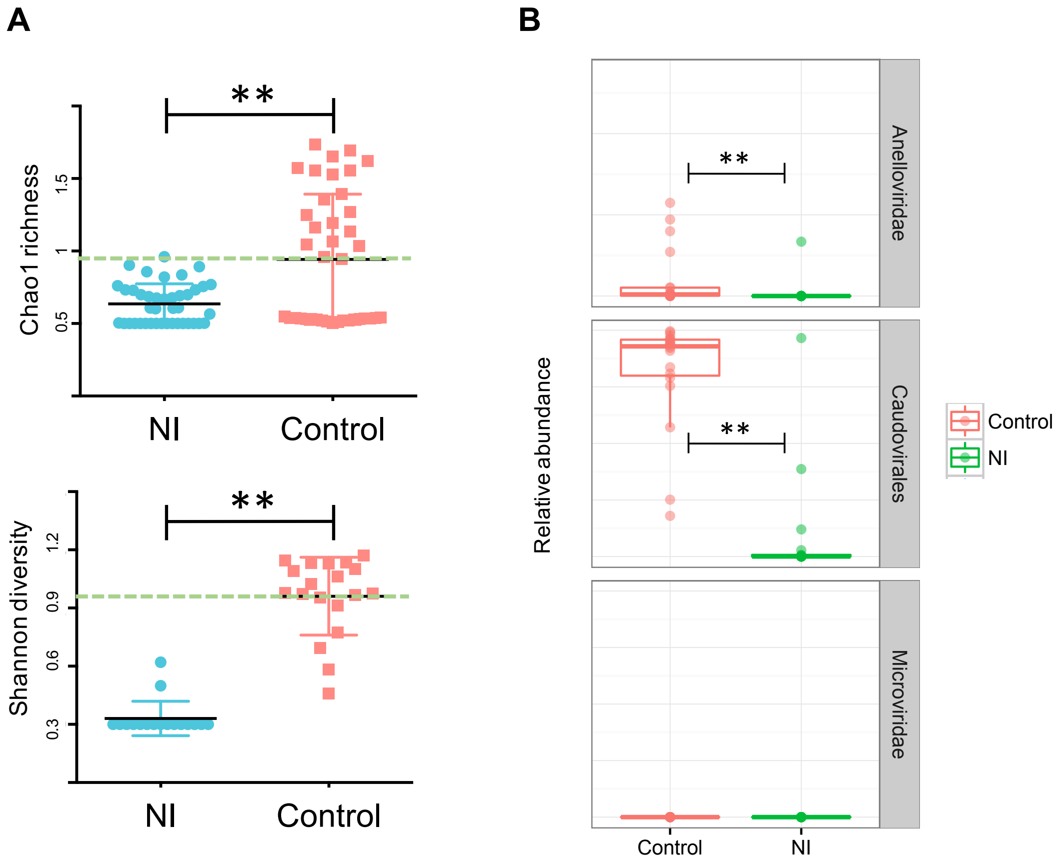


Supplementary Figure 1. Longitudinal timeline of stool sample collection (expressed in weeks). “F” indicates FMT treated subject. “D” indicates FMT donor. “S” indicates subject treated with standard therapy (STD, vancomycin). “W” indicates weeks post treatment. Red dots indicate donor samples, green dots indicate FMT recipient samples sampled at different time points.



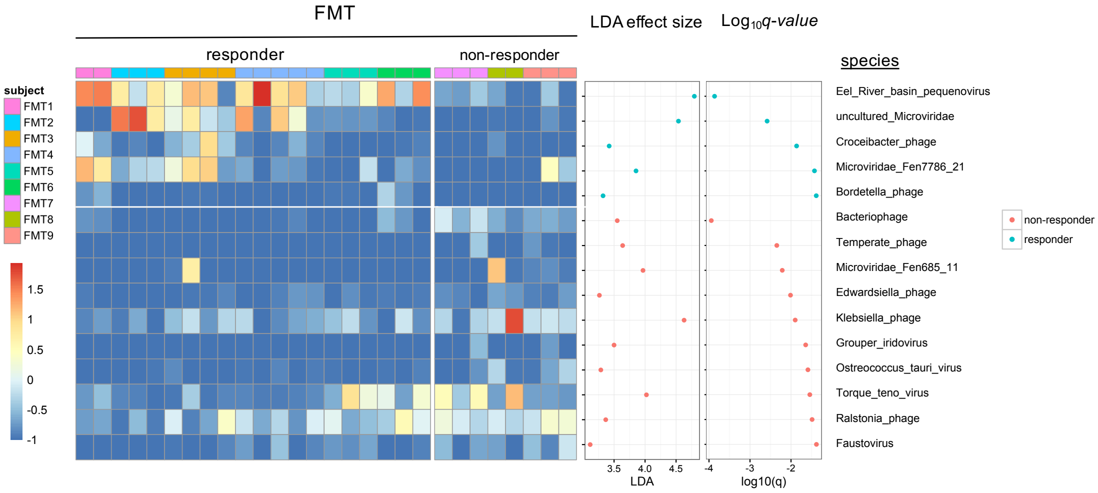
Supplementary Figure 2. Dysbiosis of the enteric virome in CDI

(A) Comparison of *Caudovirales* diversity at the contig level in CDI and controls. Statistical significance was determined by Mann-Whitney test. *$P < 0.05$. (B) Rarefaction curves of *Caudovirales* richeness, at the species level, versus an increasing number of subsamplings with replacement. (C) *Microviridae* species diversity in CDI and controls. Statistical significance was determined by Mann-Whitney test. *$P < 0.05$.



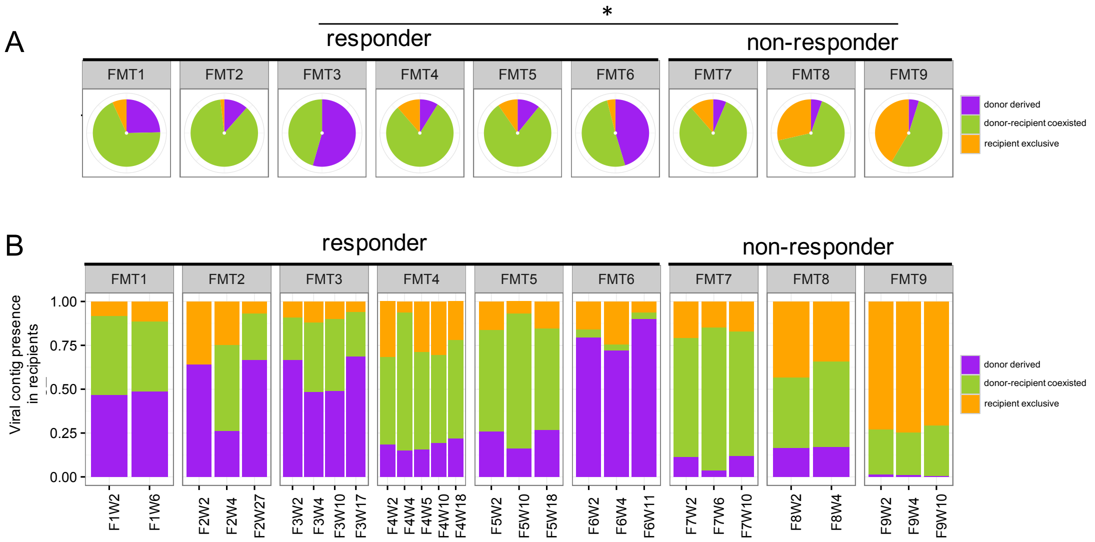
Supplementary Figure 3. Dysbiosis of the enteric virome in NI

(A) Comparison of *Caudovirales* diversity and richness between Norovirus (NI) subjects and healthy controls at the species level; (B) Relative abundances of *Caudovirales*, *Microviridae* and *Anellovirdae* in NI and healthy controls. Statistical significance was determined by Mann-Whitney test. *$P < 0.05$. NI, patients with norovirus infection.



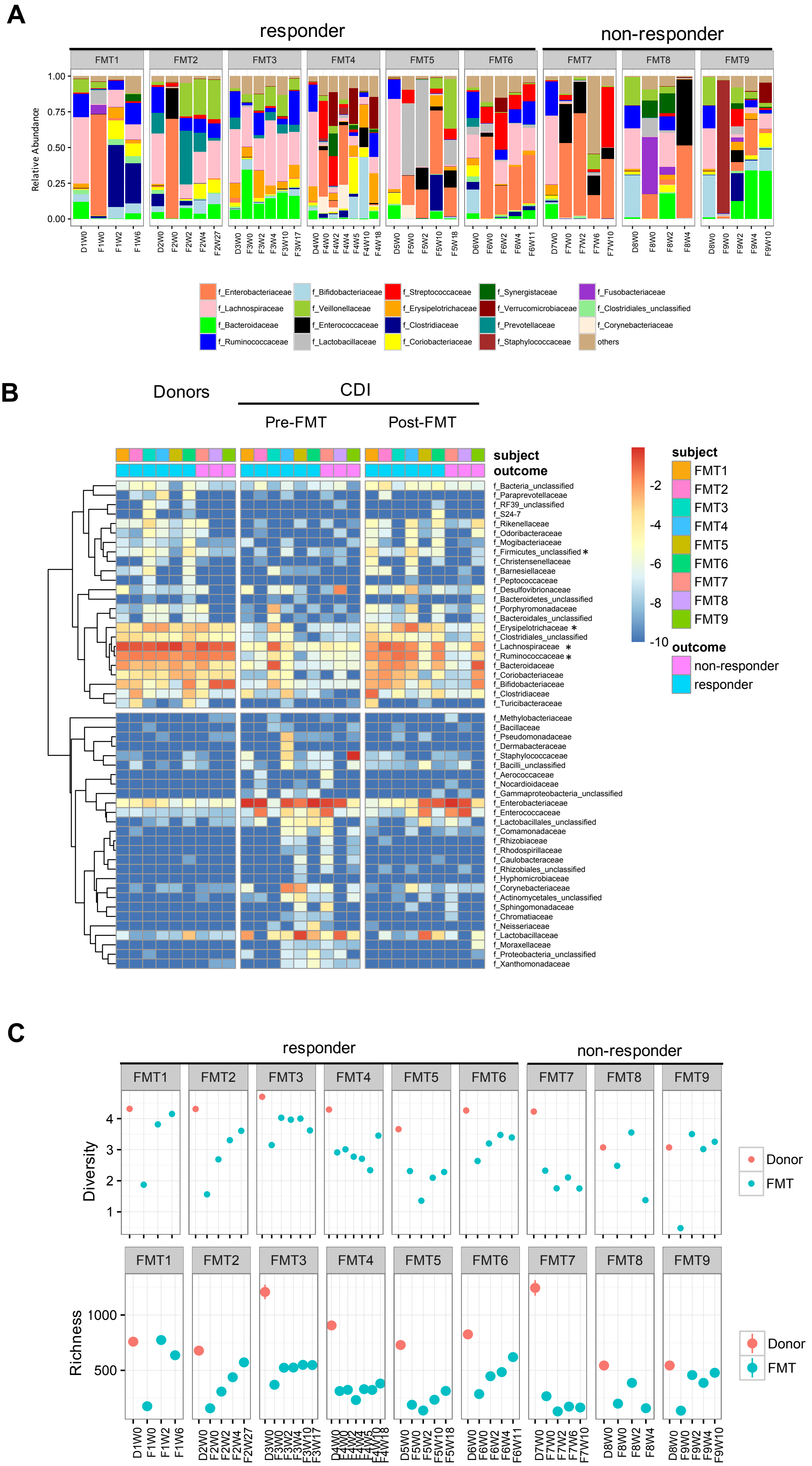
Supplementary Figure 4. Differentially enriched viral species across post-FMT samples of FMT responders versus non-responders.

Statistical significance level was determined by lefSe analysis with FDR correction. LDA effect size, q value and species annotation are shown. Green dots indicate species enriched in responders, while red dots indicate species enriched in non-responders.



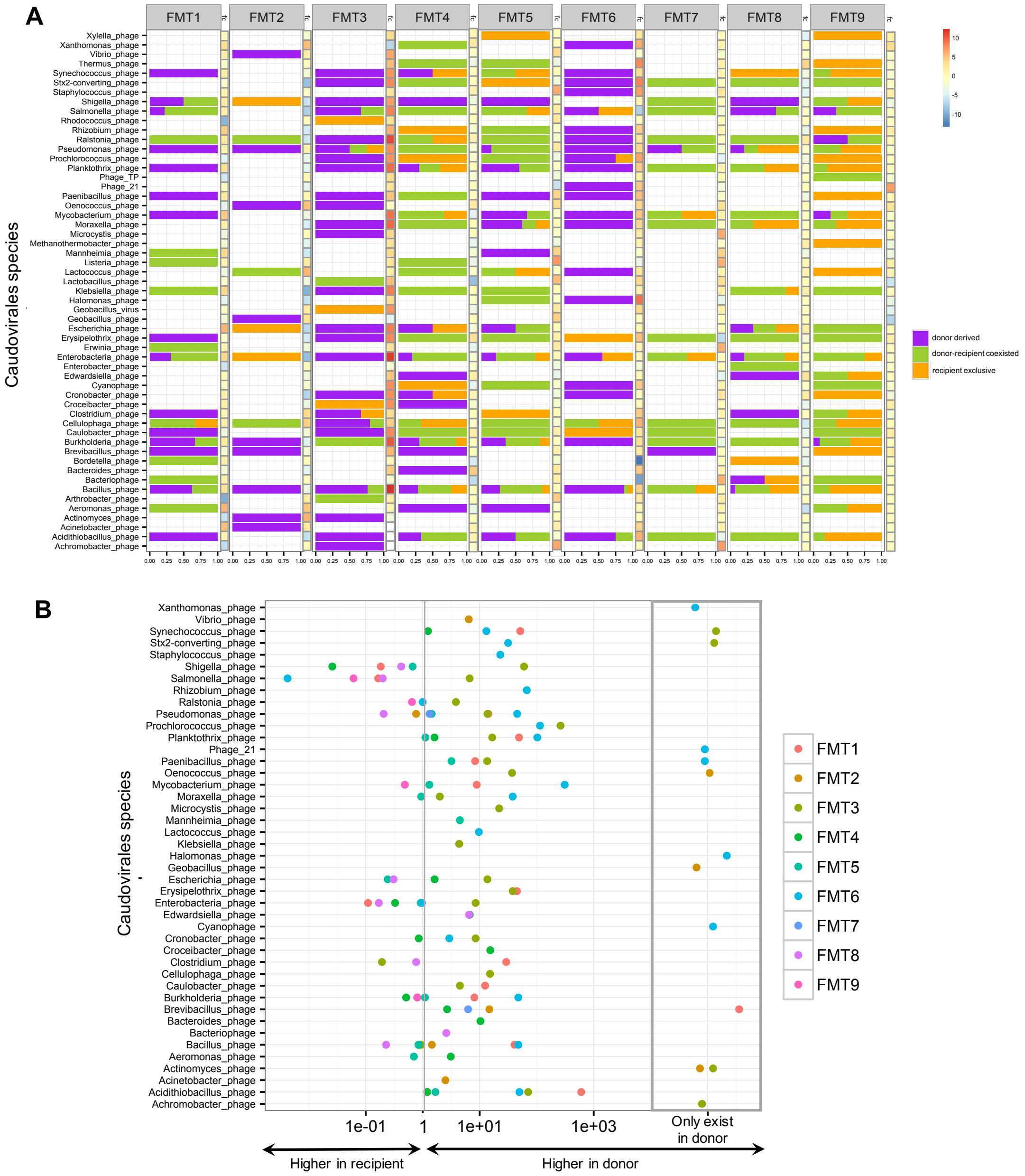
Supplementary Figure 5. Present ratio of donor transferred *Caudovirales* bacteriophages in recipients after FMT

(A) Proportion of *Caudovirales* species present in CDI subjects after FMT in the last follow-up samples. Comparison of the frequency of donor derived *Caudovirales* species in FMT responders and non-responders was determined by Mann-Whitney test. $^{*}P < 0.05$. (B) Present ratio of *Caudovirales* contigs in FMT recipients across the follow-up time period of post FMT. The color of the bar indicates the origin of the *Caudovirales* contigs. Purple indicates donor-derived contigs colonized in the recipient, orange indicates contigs exclusively present in the recipient but not in the donor, while green indicates contigs present both in donor and in recipient.


A
responder
non-responder
FMT1
FMT2
FMT3
FMT4
FMT5
FMT6
FMT7
FMT8
FMT9
Relative Abundance
1.00
0.75
0.50
0.25
0.00
D1W0
F1W0
F1W2
F1W6
D2W0
F2W0
F2W2
F2W4
F2W27
D3W0
F3W0
F3W2
F3W4
F3W10
F3W17
D4W0
F4W0
F4W2
F4W4
F4W5
F4W10
F4W18
D5W0
F5W0
F5W2
F5W10
F5W18
D6W0
F6W0
F6W2
F6W4
F6W11
D7W0
F7W0
F7W2
F7W6
F7W10
D8W0
F8W0
F8W2
F8W4
D8W0
F9W0
F9W2
F9W4
F9W10
f_Enterobacteriaceae
f_Lachnospiraceae
f_Bacteroidaceae
f_Ruminococcaceae
f_Bifidobacteriaceae
f_Veillonellaceae
f_Enterococcaceae
f_Lactobacillaceae
f_Streptococcaceae
f_Erysipelotrichaceae
f_Clostridiaceae
f_Coriobacteriaceae
f_Synergistaceae
f_Verrucomicrobiaceae
f_Prevotellaceae
f_Staphylococcaceae
f_Fusobacteriaceae
f_Clostridiales_unclassified
f_Corynebacteriaceae
others
B
Donors
CDI
Pre-FMT
Post-FMT
subject
outcome
f_Bacteria_unclassified
f_Paraprevotellaceae
f_RF39_unclassified
f_S24-7
f_Rikenellaceae
f_Odoribacteraceae
f_Mogibacteriaceae
f_Firmicutes_unclassified *
f_Christensenellaceae
f_Barnesiellaceae
f_Peptococcaceae
f_Desulfovibrionaceae
f_Bacteroidetes_unclassified
f_Porphyromonadaceae
f_Bacteroidales_unclassified
f_Erysipelotrichaceae *
f_Clostridiales_unclassified
f_Lachnospiraceae *
f_Ruminococcaceae *
f_Bacteroidaceae
f_Coriobacteriaceae
f_Bifidobacteriaceae
f_Clostridiaceae
f_Turicibacteraceae
f_Methylobacteriaceae
f_Bacillaceae
f_Pseudomonadaceae
f_Dermabacteraceae
f_Staphylococcaceae
f_Bacilli_unclassified
f_Aerococcaceae
f_Nocardioidaceae
f_Gammaproteobacteria_unclassified
f_Enterobacteriaceae
f_Enterococcaceae
f_Lactobacillales_unclassified
f_Comamonadaceae
f_Rhizobiaceae
f_Rhodospirillaceae
f_Caulobacteraceae
f_Rhizobiales_unclassified
f_Hyphomicrobiaceae
f_Corynebacteriaceae
f_Actinomycetales_unclassified
f_Sphingomonadaceae
f_Chromatiaceae
f_Neisseriaceae
f_Lactobacillaceae
f_Moraxellaceae
f_Proteobacteria_unclassified
f_Xanthomonadaceae
-2
-4
-6
-8
-10
subject
FMT1
FMT2
FMT3
FMT4
FMT5
FMT6
FMT7
FMT8
FMT9
outcome
non-responder
responder
C
responder
non-responder
FMT1
FMT2
FMT3
FMT4
FMT5
FMT6
FMT7
FMT8
FMT9
Diversity
4
3
2
1
Donor
FMT
Richness
1000
500
Donor
FMT
D1W0
F1W0
F1W2
F1W6
D2W0
F2W0
F2W2
F2W4
F2W27
D3W0
F3W0
F3W2
F3W4
F3W10
F3W17
D4W0
F4W0
F4W2
F4W4
F4W5
F4W10
F4W18
D5W0
F5W0
F5W2
F5W10
F5W18
D6W0
F6W0
F6W2
F6W4
F6W11
D7W0
F7W0
F7W2
F7W6
F7W10
D8W0
F8W0
F8W2
F8W4
D8W0
F9W0
F9W2
F9W4
F9W10

Supplementary Figure 6. Alterations in the bacterial microbiome over the course of post-FMT follow-up

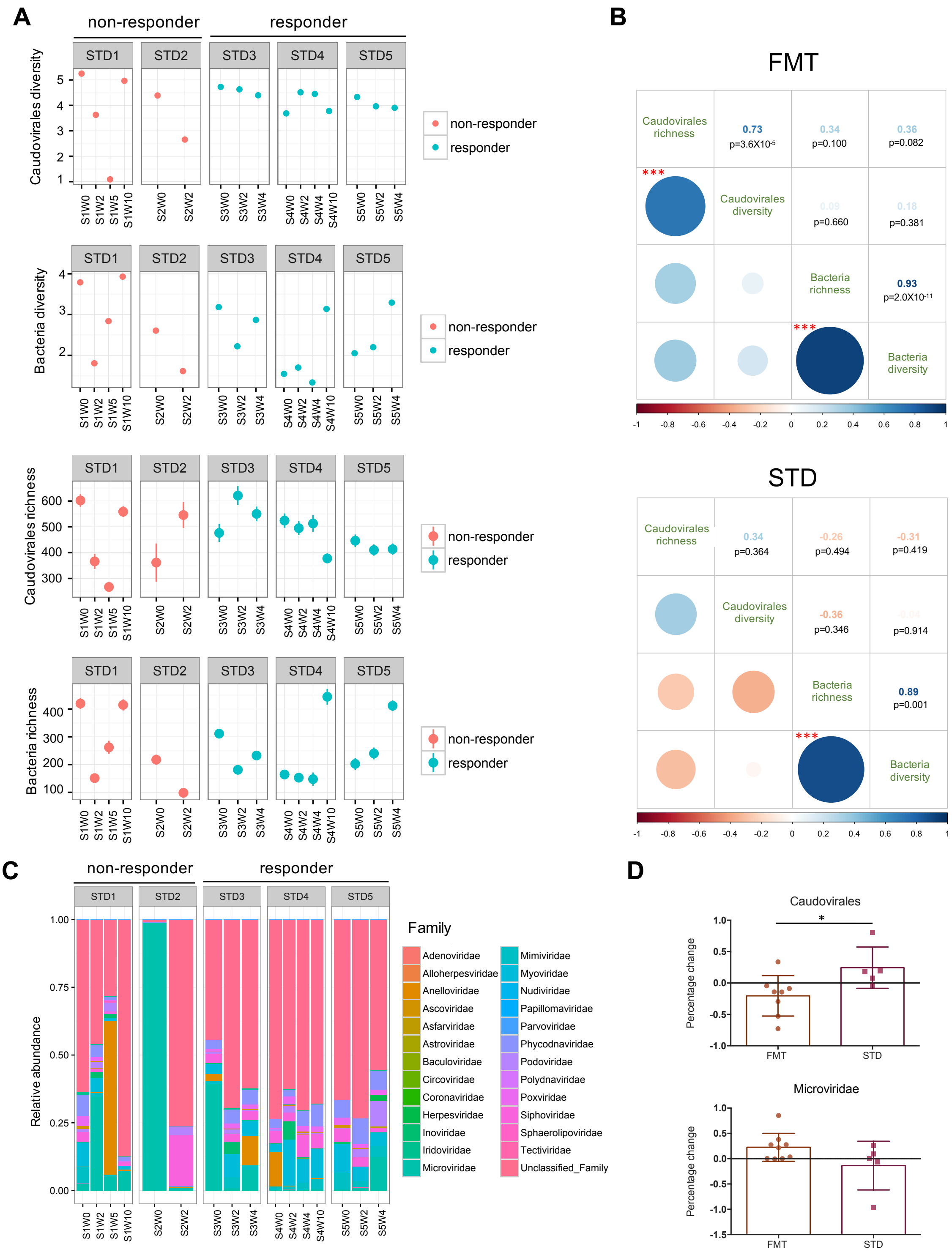
(A) Changes of the relative abundance of top19 bacterial families in the follow-up stool samples of FMT recipients. “F” indicates FMT recipient. “D” indicates FMT donor. “W” indicates weeks post treatment. (B) Heatmap of the abundance of differentially presented bacterial families in donor, pre-FMT and post-FMT last follow-up samples. Bacterial families with significant changes post FMT are labeled with aterisk. (C) Plots of bacterial Shannon diversity (top) and Chao1 richness (bottom) in the follow-up stool samples of FMT recipients and their corresponding donor.



Supplementary Figure 7. Transfer of donor contigs with respect to each *Caudovirales* species and its relationship with post-FMT abundance alterations and donor species abundances

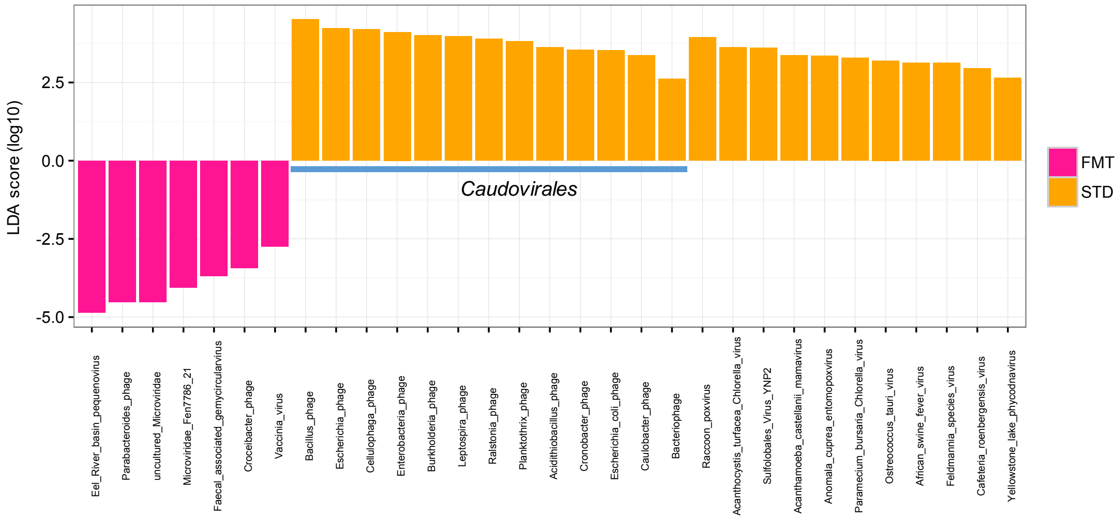
(A) Proportion of presence of contigs within each *Caudovirales* speices in the last follow-up samples after FMT, as depicted in the horizontal bars, and heatmap of the post FMT alterations of *Caudovirales* species abundance, as depicted in the vertical bars. “fc” stands for log2 transformed fold change post FMT. The color of the bar indicates the origin of the *Caudovirales* contigs. Purple indicates donor-derived contigs colonized in the recipient, orange indicates contigs exclusively present in the recipient but not in the donor, while green indicates contigs present both in donor and in recipient.

(B) Donor-to-recipient ratios of the relative abundance of each *Caudovirales* species as calculated as the relative abundance of *Caudovirales* species in donor divided by the relative abundance of *Caudovirales* species in recipient before FMT.



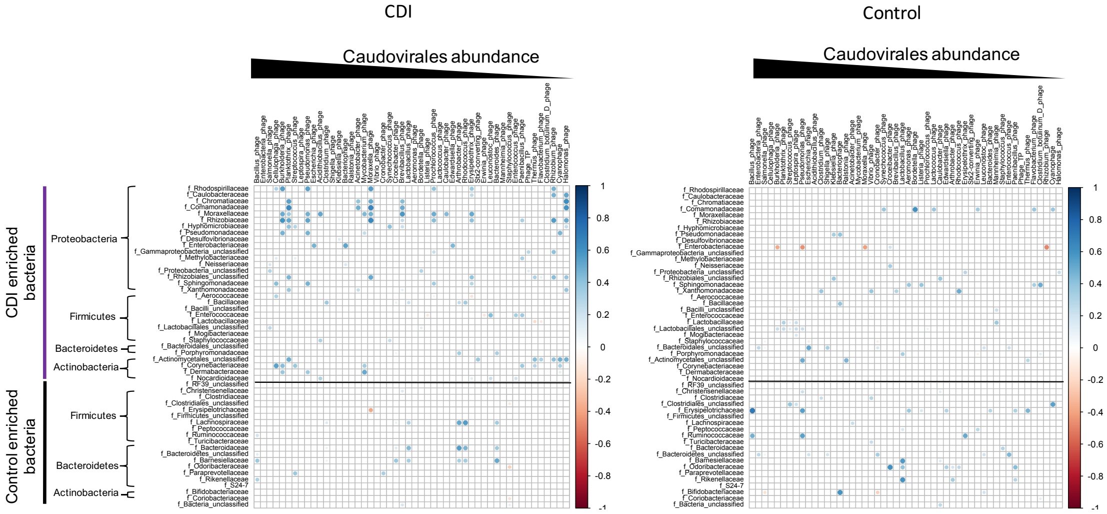
Supplementary Figure 8. Alterations in the diversity and richness of *Caudovirales* virome and bacterial microbiome in patients treated with vancomycin. (A) Diversity (Shannon) and richness (Chao1) alterations of the *Caudovirales* virome and bacterial microbiome in stool samples of CDI patients after vancomycin treatment (STD) up to last follow-up. “S” indicates subject treated with vancomycin (standard therapy, STD). “W” indicates weeks post treatment. (B) Spearman correlation plots of bacteria-

Caudovirales relationship pattern across vancomycin treatment (STD) and FMT follow-up samples respectively. Statistical significance was determined for all pairwise comparisions, significant correlations (P value < 0.05) are displayed with asterisk. Blue circles and positive values indicate positive correlations, red circles and negative values indicate inverse correlations. The size and shading indicate the magnitude of the correlation where darker shades are more correlated than lighter ones. (C) Virome community structure changes over the course of vancomycin at the family level. (D) Change in the relative abundance of *Caudovirales* and *Microviridae* after treatment with FMT and vancomycin (STD). Statistical significance was determined by Mann-Whitney test. *$P < 0.05$.



Supplementary Figure 9. Differentially enriched viral species in FMT and STD treated patients after treatment.

Patients with treatment responses were compared by LefSe analysis across all the corresponding follow-up samples between FMT responders and STD responders. Only taxa with LDA score >2 and q value <0.05 are shown.



Supplementary Figure 10. Spearman correlation plots of the relative abundances of *Caudovirales* species and bacterial families identified to be significantly associated with CDI and controls.

Statistical significance was determined for all pairwise comparisons; only significant correlations (p value < 0.05) are displayed. Statistical significance was determined for all pairwise comparisons; significant correlations (p value < 0.05) are displayed with asterisk. Blue circles and positive values indicate positive correlations, red circles and negative values indicate inverse correlations. The size and shading indicate the magnitude of the correlation where darker shades are more correlated than lighter ones.

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