

## SUPPLEMENTARY DISCUSSION

### The value of purifying VLPs for viral metagenomic projects

When each of the 32 fecal VLP-associated viromes, sequenced to an average depth of  $7.8 \pm 2.9$  Mb (per sample) was used to query the 12 microbiomes sampled to an average depth of  $92.2 \pm 17.5$  Mb, we noted that  $55.8 \pm 32.4$  % (mean  $\pm$  SD) of viral sequences generated from the VLP preps from a given human host were detectable in that individual's sequenced fecal microbiome. When a deeply sampled VLP-virome (70.16 Mb) was used to query 0.91 Gb of pyrosequencer reads from the corresponding deeply sequenced fecal microbiome<sup>15</sup>, the percentage of VLP-derived sequences found in the fecal community DNA sample was 76.14% (**Fig. S15**). Using the same BLAST E-value threshold cutoff, we performed a reciprocal analysis, asking what percentage of the total sequences present in each of the microbiome datasets matched to sequences present in VLP datasets generated from fecal samples collected from that human host. The results disclosed that viral reads represented  $3.5 \pm 2.2$ % (mean  $\pm$  SD) of total fecal community DNA sequences in the case of the 12 more shallowly sequenced microbiomes, and 2.5% in the case of the deeply sequenced microbiome and its corresponding deeply sequenced virome (**Fig. S15a**). These findings support a view that at the present time isolating VLPs is an efficient and direct way to characterize phage populations associated with a given (fecal) microbial community.

### CRISPRs

Clusters of Interspaced Short Palindromic Repeats (CRISPR) elements are stretches of DNA composed of short palindromic repeats (23-47bp) that flank short "spacers" composed of viral DNA; their presence in a bacterial genome represents a key component of host defense against bacteriophage attack<sup>1,2</sup>. We used CRISPR-Finder<sup>37</sup> to search sequenced human gut microbial genomes; CRISPR elements were detected in 48 of 74 human gut bacterial species queried and in a prominent human gut archaeon

(*Methanobrevibacter smithii*) (see **Table S9** for the list of genomes). We identified a total of 95 different direct repeats and 2,196 different spacers. These direct repeats were subsequently used to interrogate the fecal microbiome datasets to identify reads that contained at least two copies of the same direct repeat. The spacers interposed between these repeats were subsequently extracted, and together with the spacers from the 121 sequenced human gut microbial genomes used to search for sequences with high similarity in VLP viromes (defined by Cross\_match; maximum of 1 gap allowed and similarity over  $\geq 90\%$  of its length). This effort yielded 1,262 reads that were similar ( $\geq 90\%$  identity) to a spacer sequence. Sixteen of the 38 VLP viromes (including technical replicates of samples from members of families F1-4 and the deeply sequenced virome) had hits to spacers derived from fecal microbiomes. In the 12 sequenced fecal community microbiomes for which there were corresponding VLP preparations, the only hits to the viromes were spacers represented in another individual's microbiome (**Table S11**). In this analysis of fecal microbiome datasets from a single time point, and at this depth of shotgun sequencing of the microbiome, the absence of detectable viral sequences with significant similarity to bacterial spacers in a given individual's fecal microbiome suggests that viruses to which their bacterial communities were resistant are not represented in the corresponding VLP preparation. If temperate phage dominate in the fecal microbiome, we would not expect such resistance to appear at least as judged by the representation of CRISPR spacers in viromes and microbiomes. However, additional and deeper shotgun datasets of total fecal microbial community DNA need to be generated from samples collected at all time points surveyed for each individual in order to further assess whether resistance does or does not occur.

### **Eukaryotic viruses represented in VLP viromes**

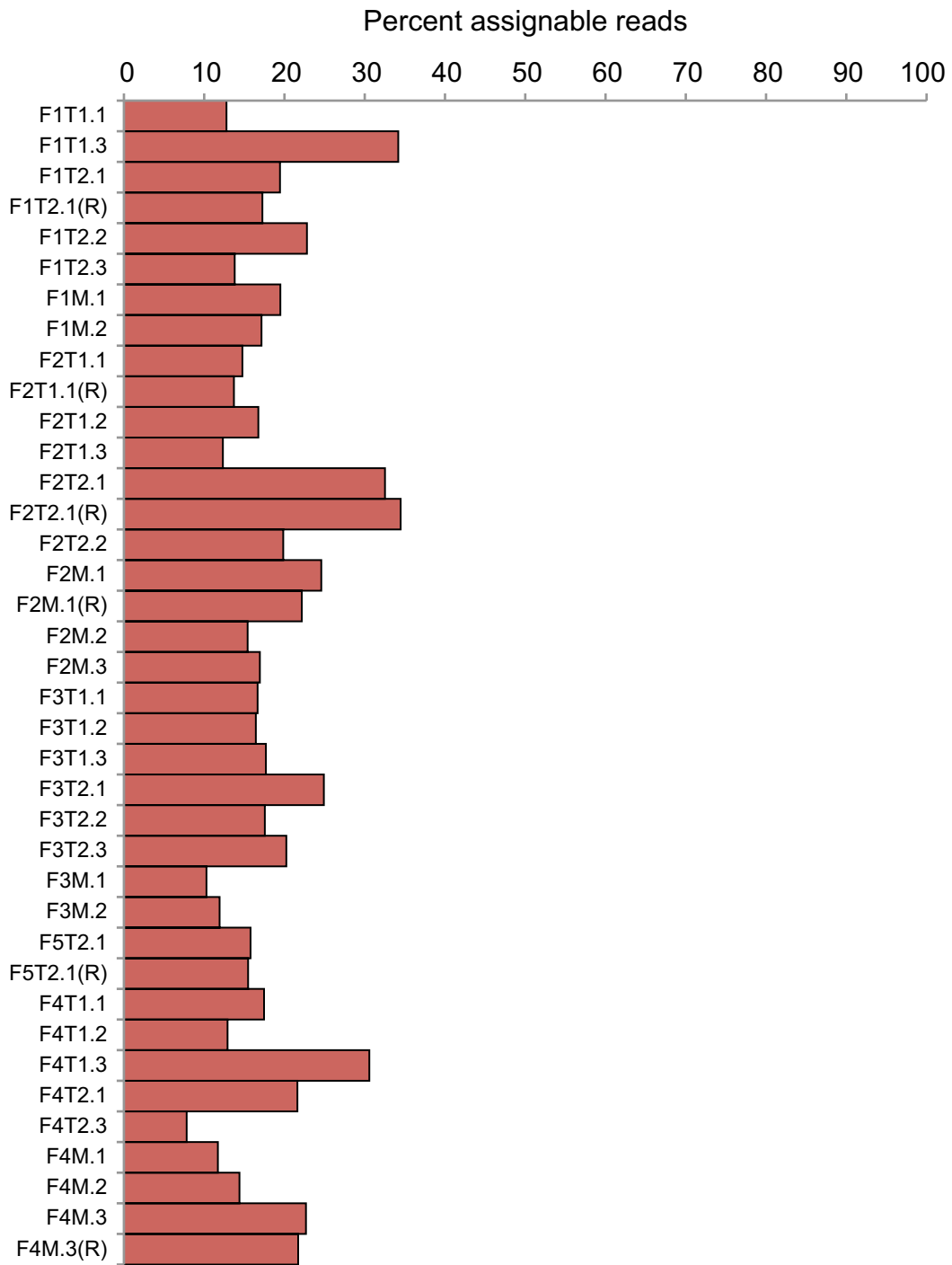
Although 73% of the sequences in the NR\_Viral\_DB belong to eukaryotic viruses, none of the VLP samples yielded reads covering more than 50% of the genome

of any known eukaryotic virus (tblastx, e-value < 1e-3). Eukaryotic viruses with hits throughout more than 20% of their genomes included: (i) six non-human Herpesviridae with 22–49% genome coverage; (ii) one Maculavirus (Grapevine\_fleck\_virus; 39% coverage of its 7,564bp genome); (iii) one Aquareovirus (Aquareovirus\_A\_segment\_11; 26% coverage of this 783bp segment of its genome); (iv) one Parapoxivirus (Bovine\_papular\_stomatitis\_virus; 22% coverage of its 134,431bp genome); and (v) one human Rotavirus (Human\_rotavirus\_G3\_segment\_11; 21% coverage of this 1,043bp genome segment).

## Supplementary Figures and Legends

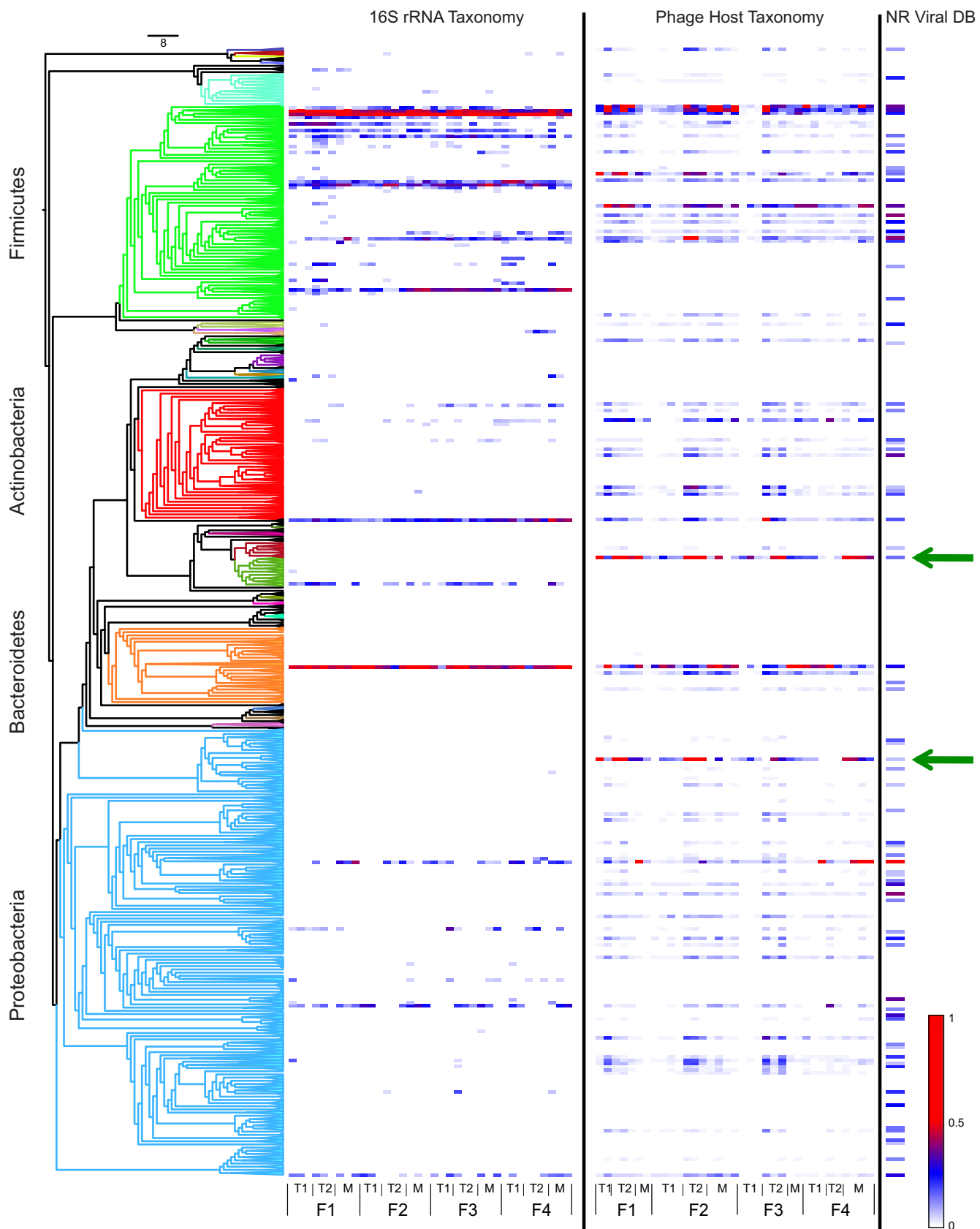
**Fig. S1. Percent of pyrosequencing reads generated from VLP preparations that map to the NR\_Viral\_DB.** Sample-by-sample distribution of the percentage of VLP-derived reads with hits (tblastx, e-value < 1e-3) to the NR\_Viral\_DB. See the legend to **Fig. 1** in the main text for an explanation of the nomenclature used to designate samples.

Reyes *et al.*, Supplementary Fig. 1



**Fig. S2. Correlating family-level bacteria taxa present in fecal samples with the known bacterial hosts of bacteriophage present in the NR\_Viral\_DB and their identified homologs in fecal VLP metagenomic datasets.** The Universal Bacterial 16S rRNA tree in Greengenes was downloaded ([http://greengenes.lbl.gov/Download/Taxonomic\\_Outlines/](http://greengenes.lbl.gov/Download/Taxonomic_Outlines/)), collapsed at a family level based on NCBI taxonomy, and branches colored according to their assigned phyla. The left panel corresponds to distribution and relative abundance (1.0 = most abundant) of the different samples according to 16S rRNA data. The middle panel shows the distribution and percent coverage of bacteriophage genomes from the NR\_Viral\_DB by VLP-derived reads; phage genomes are classified according to their host taxonomy. The right panel shows the distribution and relative abundance of the known bacterial hosts of phage present in the NR\_Viral\_DB. Columns are sorted by individual and time points of fecal sampling. Green arrows point to ssDNA phage from *Chlamydia* and *Bdellovibrio* known to be preferentially amplified by WGA methods<sup>17</sup>. For sample abbreviations see **Fig 1** in the main text.

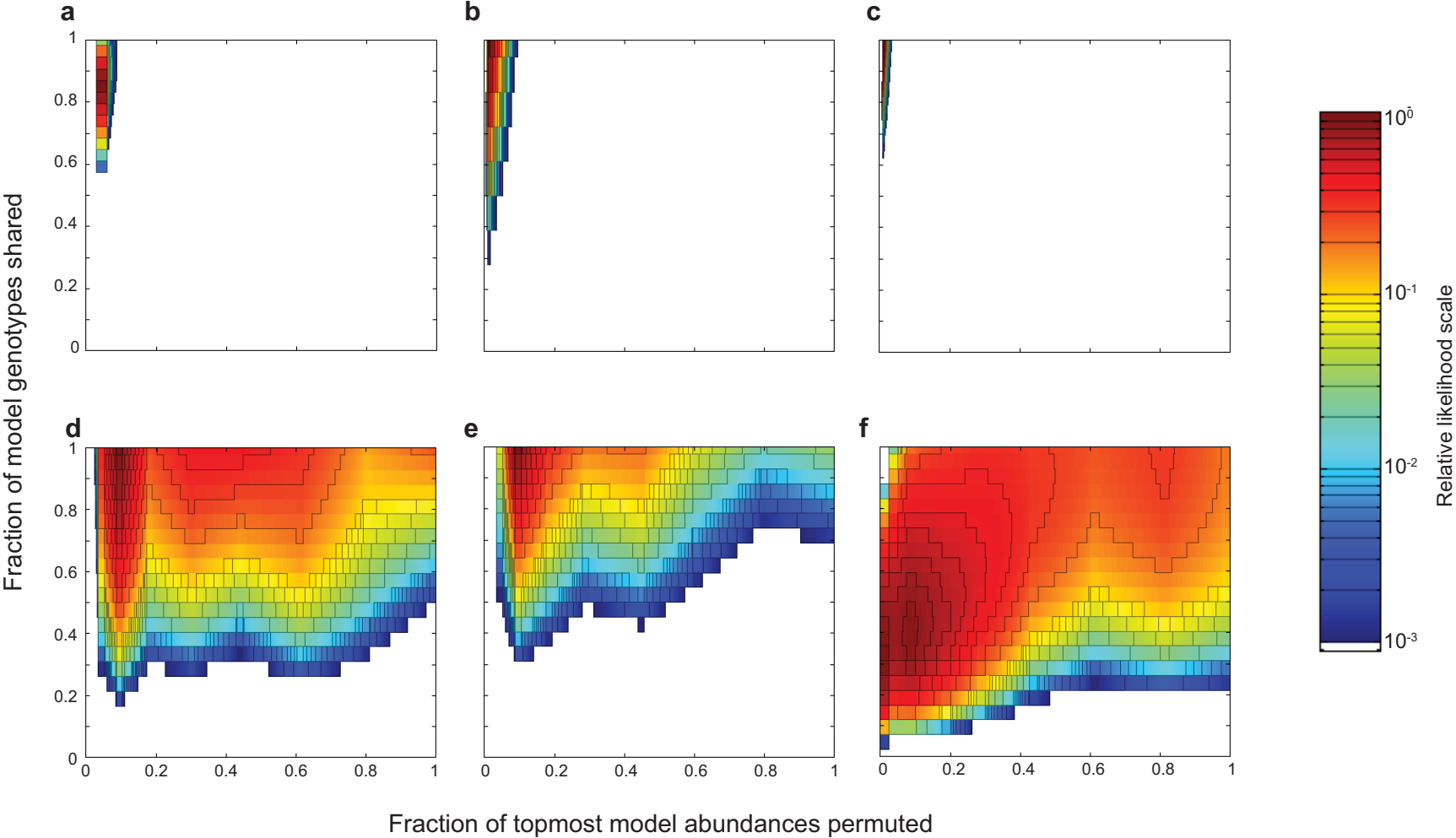
Reyes *et al.*, Supplementary Fig. 2



**Fig. S3. Representative Monte Carlo simulations for cross contigs defining intrapersonal vs interpersonal variation in VLP DNA viromes.** Monte Carlo simulations for the percent shared viral genotypes (virotypes) and percent permuted rank abundance of virotypes between pairs of fecal VLP samples. Colors indicate the likelihood score for a given position. Intra-personal variation is displayed in panels a-c: F4T3.2 vs F4T3.3 (a); F2T1.1 vs F2T1.3 (b); F1T2.2 vs F1T2.3 (c). Inter-personal variation is illustrated in panels d-f: F3M vs F3T1 (d); F2T1 vs F2T2 (e); F4T1 vs F4T2 (f).

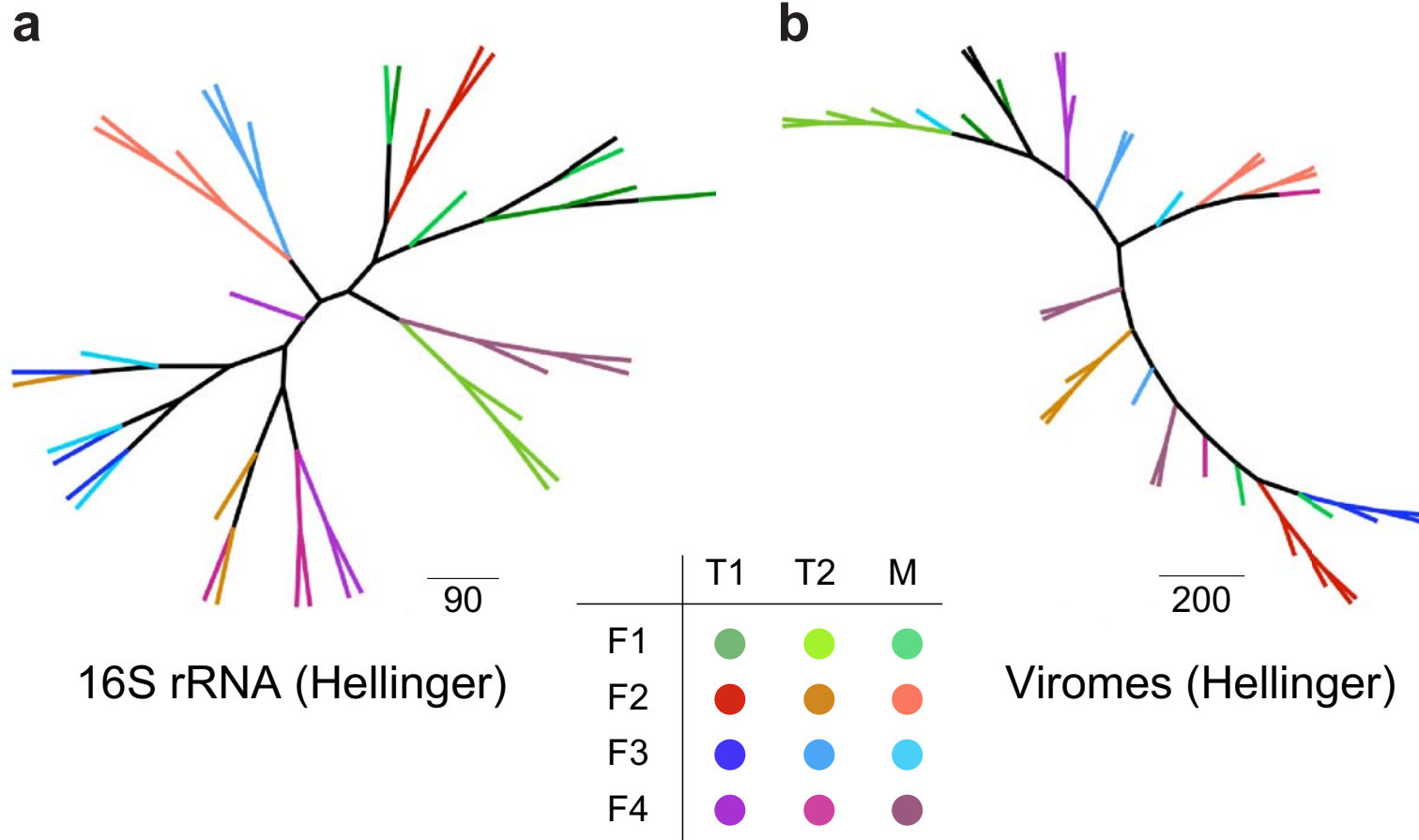


Reyes *et al.*, Supplementary Fig. 3



**Fig. S4. Beta-diversity analysis: clustering of fecal VLP-associated viromes and bacterial 16S rRNA data.** Unrooted, jack-knifed (100 iterations) consensus UPGMA trees obtained from Hellinger-based distance matrices are shown for bacterial 16S rRNA data (a) and VLP-derived viromes (b). The color key provides information about the family (F), and family member. Bars represent Hellinger distances.

Reyes *et al.*, Supplementary Fig. 4

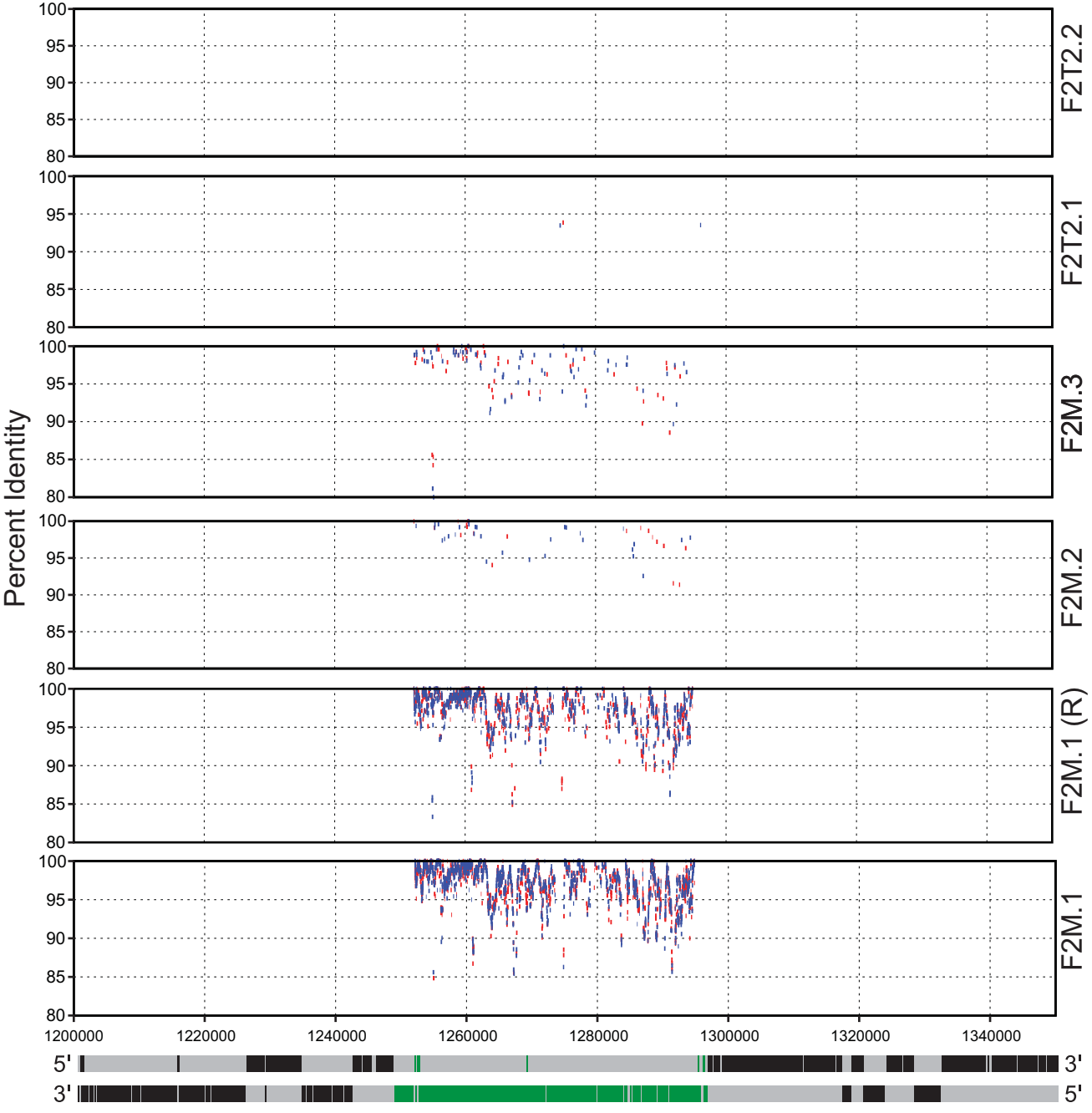


**Fig. S5. Beta-diversity analysis.** Branch support for the trees displayed in **Fig. S4**. Hellinger-based UPGMA trees for bacterial 16S rRNA data and VLP-derived viromes are displayed in panels a and b, respectively. The color key provides information about family (F) and the family member.



**Fig. S6. Percent similarity plots of VLP virome reads mapping to a predicted prophage in *Ruminococcus torques* ATCC 27756.** The genes present within the ~60 Kbp prophage are shown in green, and those present on either strand of the flanking bacterial genome are shown in black at the bottom of the figure. Pyrosequencer reads, generated from fecal VLPs, prepared at 2 or more time points from a co-twin (T2) and her mother (M) belonging to family 2 (F2) and having  $\geq 80\%$  identity with prophage genes, are displayed as blue dots (each dot represents a single read with a hit to the positive strand of the prophage) or red dots (negative strand hits)

Reyes *et al.*, Supplementary Fig. 6

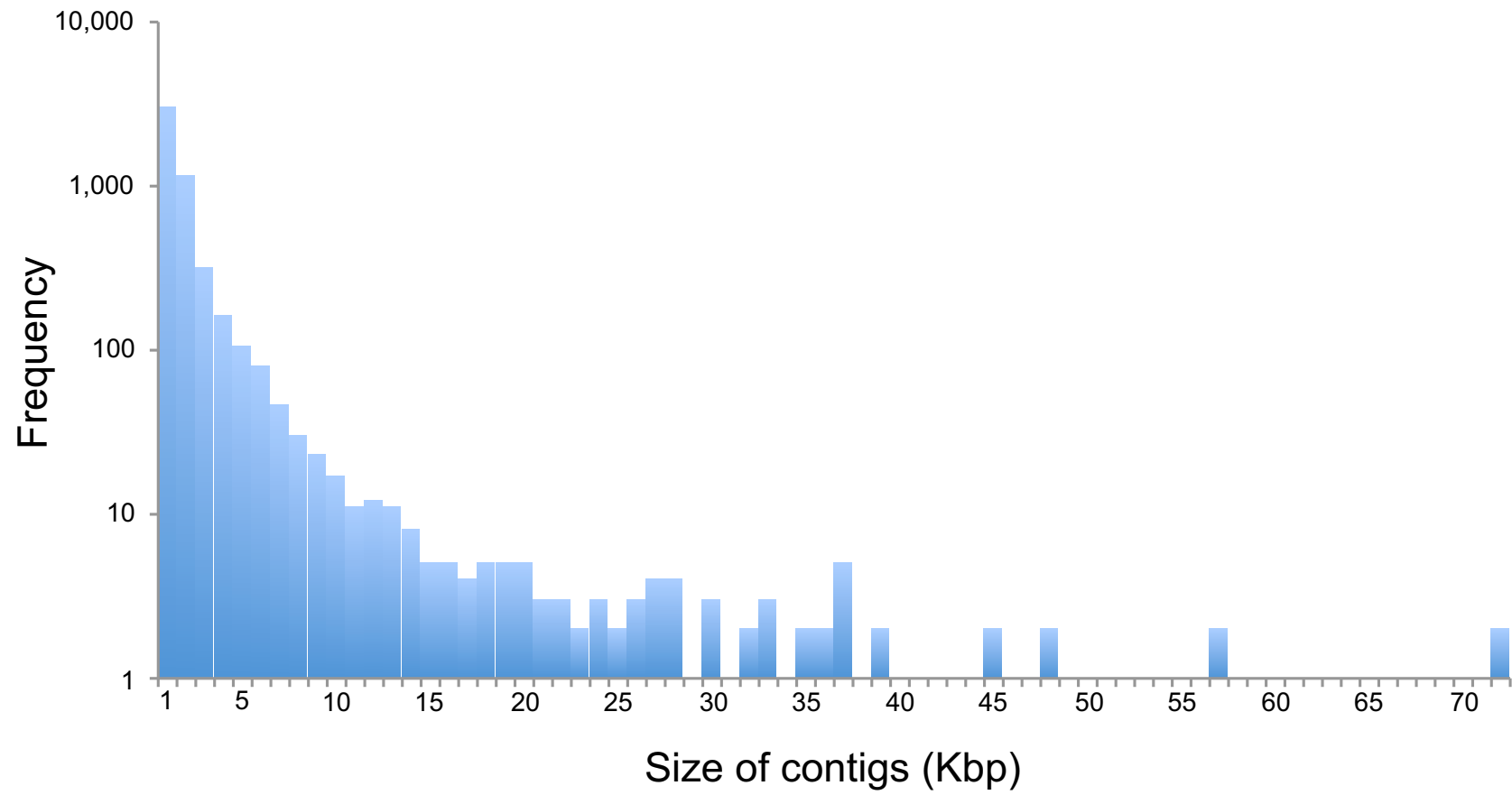


*Ruminococcus torques* ATCC 27756

**Fig. S7. Length distribution of viral contigs assembled from VLP-derived pyrosequencing reads.** A frequency histogram of contig length is shown.

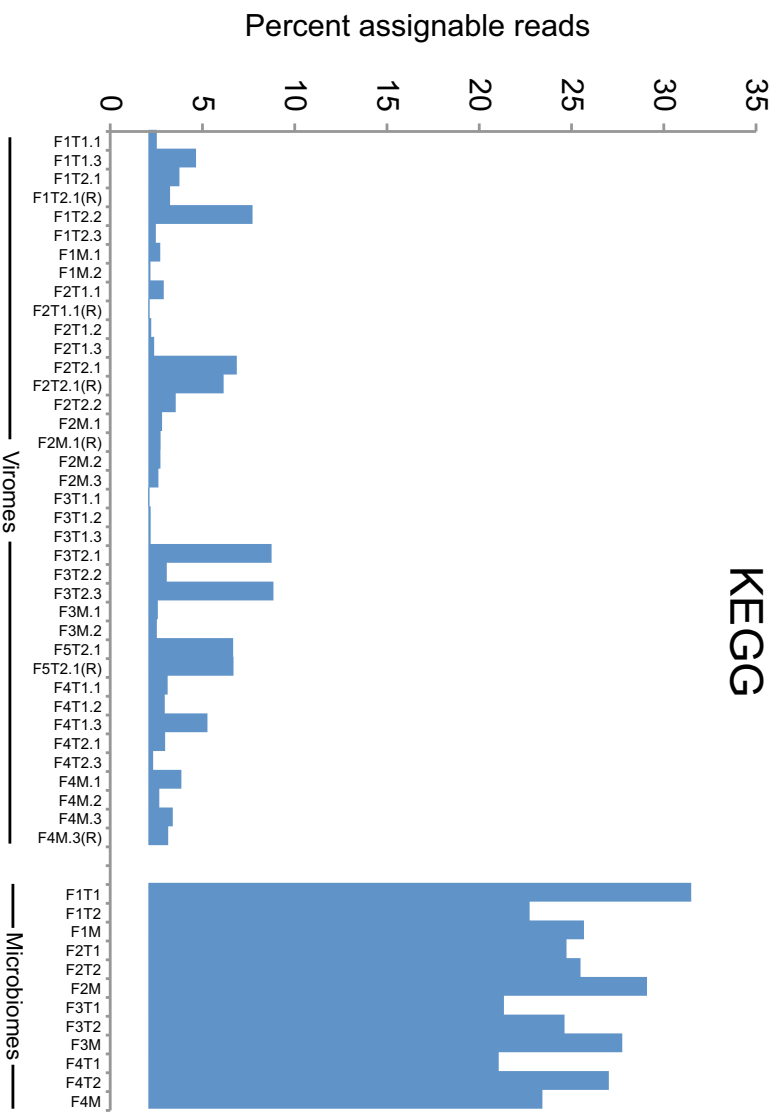
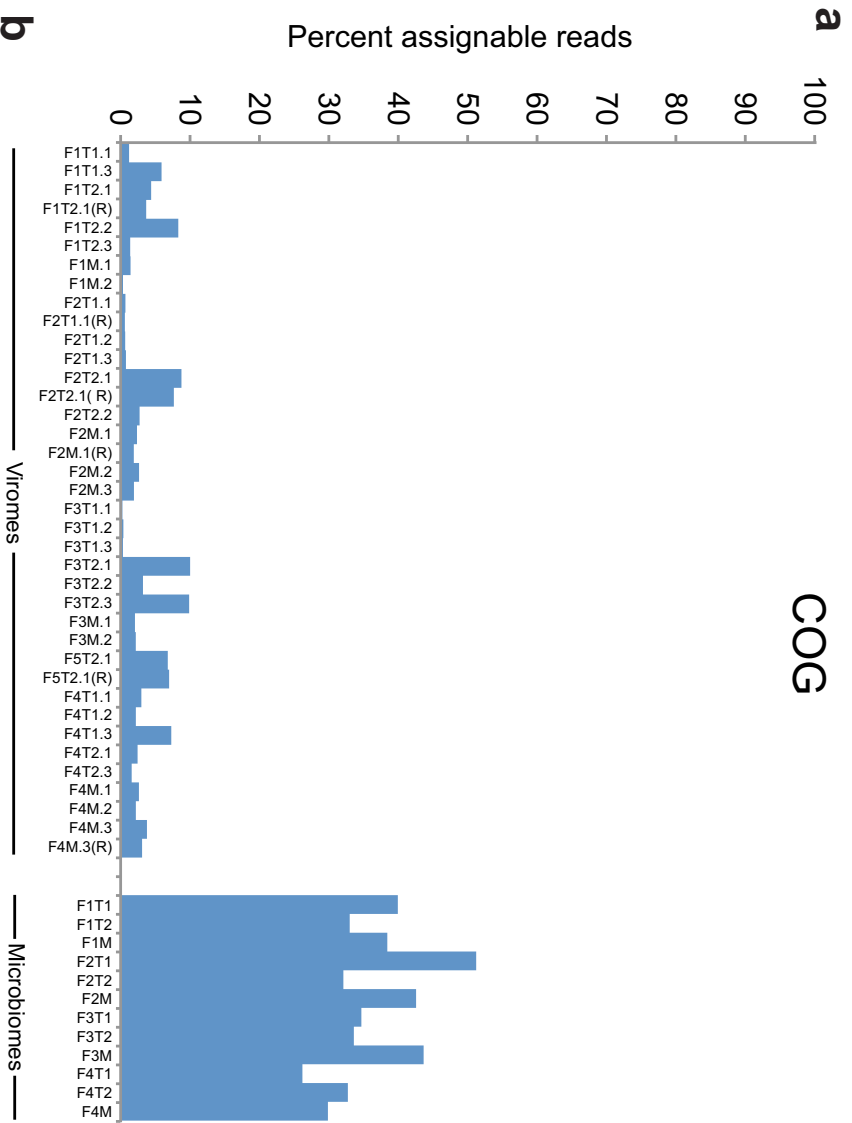


Reyes *et al.*, Supplementary Fig. 7



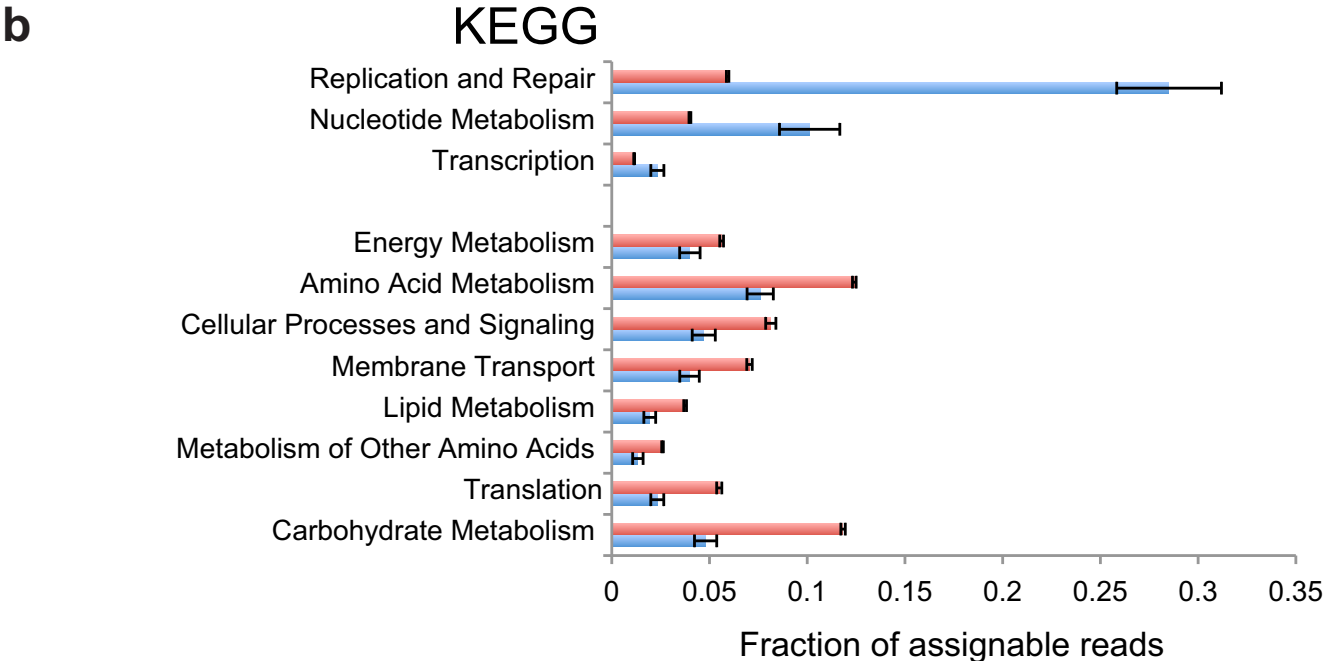
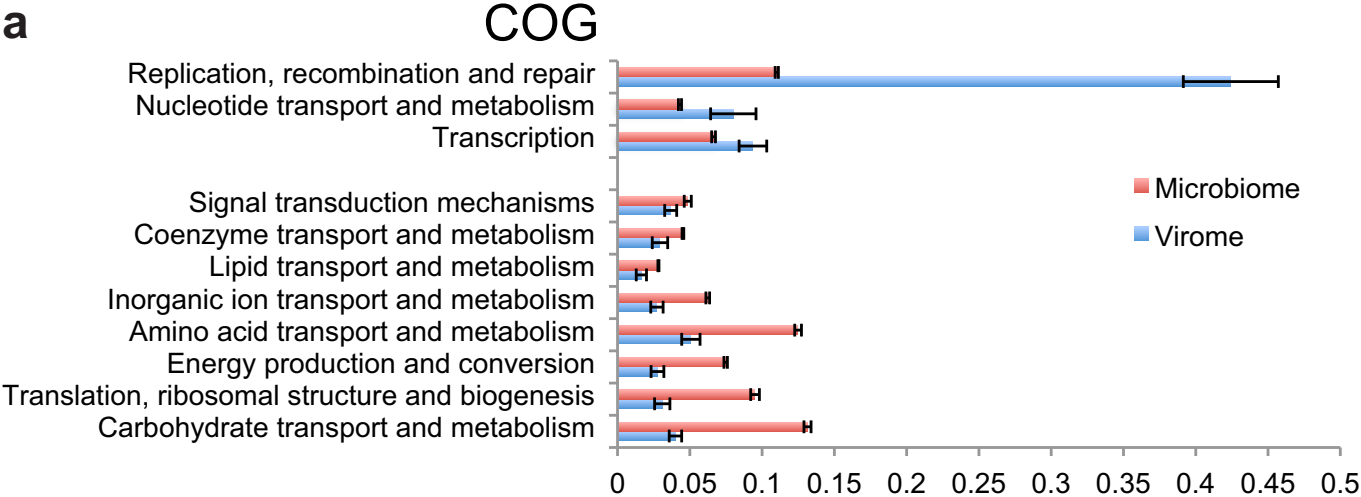
**Fig. S8. Percentage of fecal virome and microbiome reads with significant hits to COG categories and KEGG second level pathways.** Sample by sample percentage of reads with significant hits (blastx, e-value cutoff  $<1e-5$ ) to (a) COG (STRING v7) and (b) KEGG (v44) databases.

**Reyes et al., Supplemental Fig. 8**



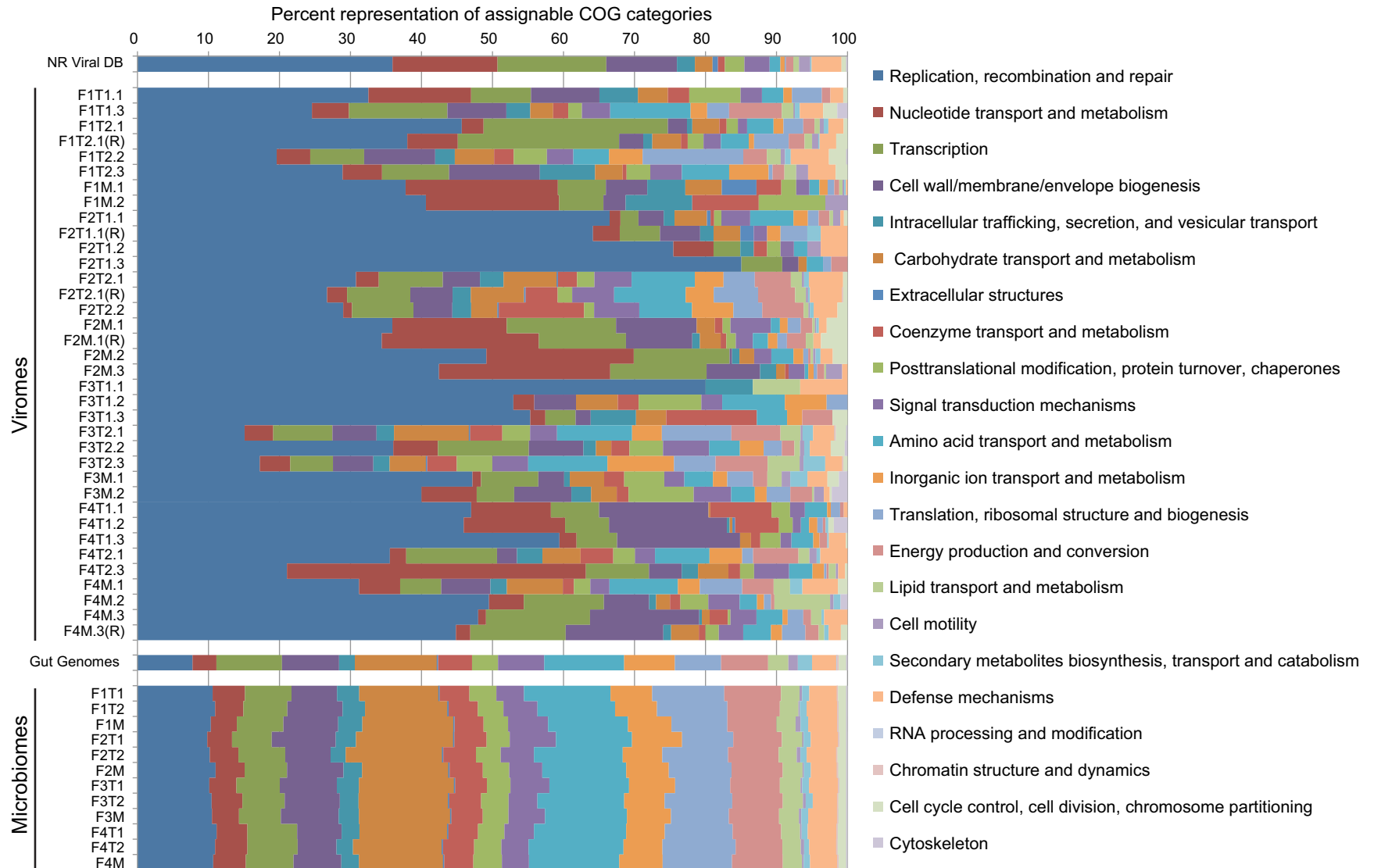
**Fig. S9. KEGG and COG annotations reveal significant differences in functions between fecal VLP-associated viromes and microbiomes.** Only COG-categories (panel a) and KEGG second level pathways (panel b) with significant differences in their representation between fecal microbiomes and VLP-associated viromes are shown (mean  $\pm$  s.e.m plotted;  $p < 0.05$ ; two sample t-test calculated using Metastats).

Reyes *et al.*, Supplementary Fig. 9



**Fig. S10. A sample-by-sample view of the proportional representation of COG categories in sequenced VLP-associated viromes and gut microbiomes.** Blastx assignment (e-value cutoff  $<1e-5$ ) of reads to functional categories. Shown from top to bottom are proteins from viruses in the NR\_Viral\_DB and fecal VLP-derived viromes, plus proteins from 121 sequenced human gut-associated microbial genomes and fecal microbiomes. See **Fig. 1** for sample nomenclature.

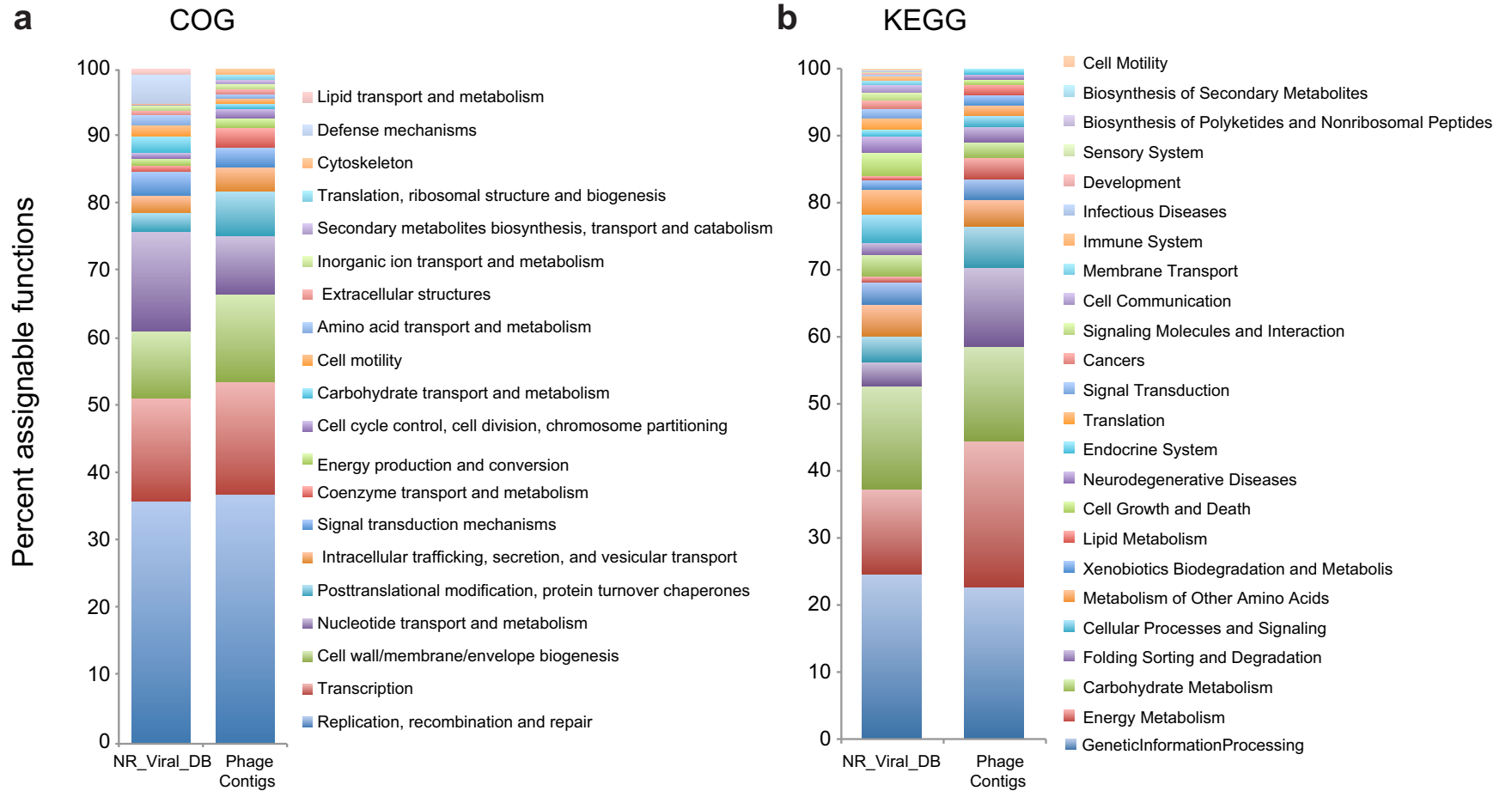
Reyes *et al.*, Supplementary Fig. 10



**Fig. S11. Comparison of the representation of KEGG and COG groups in proteins encoded by large VLP-derived contigs and in the NR\_Viral\_DB.** Searches (blastp, e-value  $<1e-5$ ) were performed against the STRING COG database (panel a) and KEGG (results for second level pathways are shown in panel b).



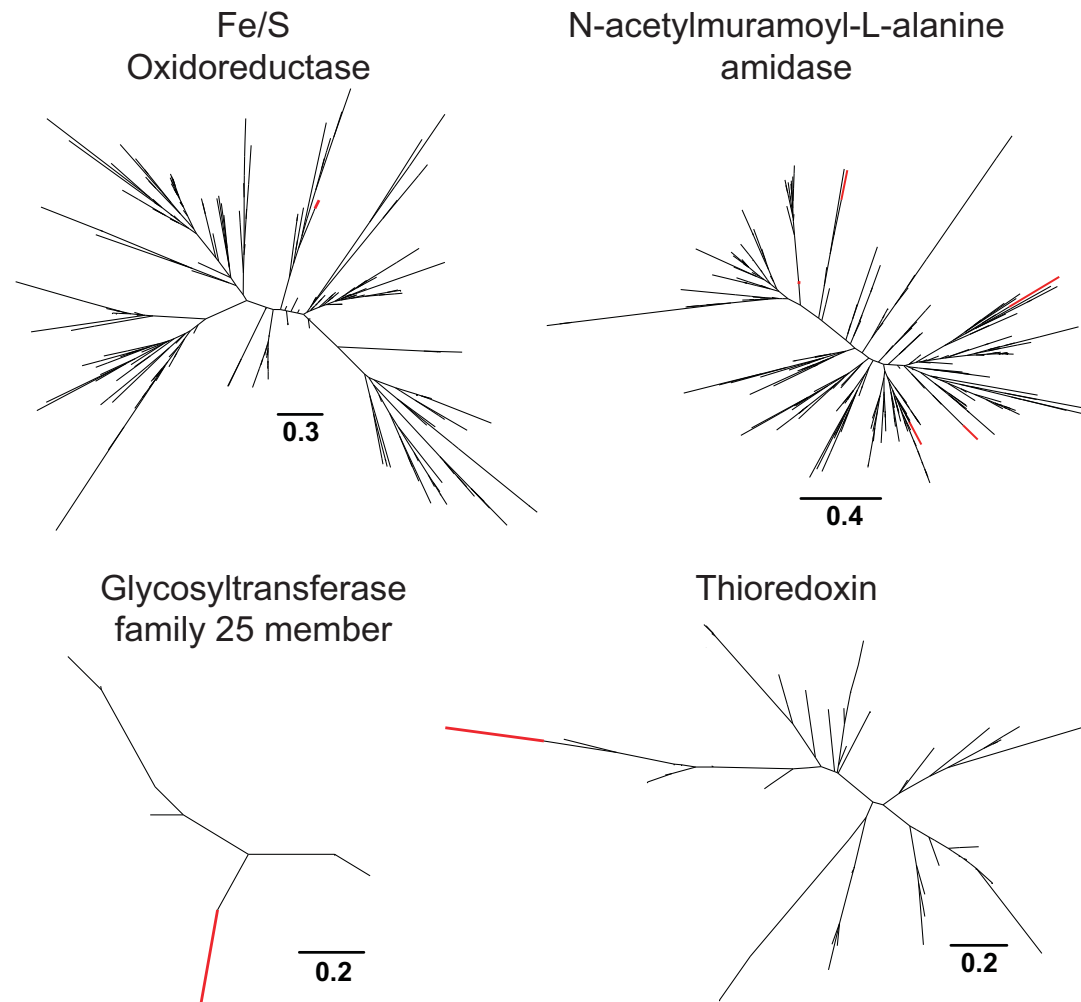
Reyes *et al.*, Supplementary Fig. 11



**Fig. 12. Representative phylogenetic trees of bacterial proteins present in large contigs assembled from VLP-viromes with no homologs in the NR\_Viral\_DB.**

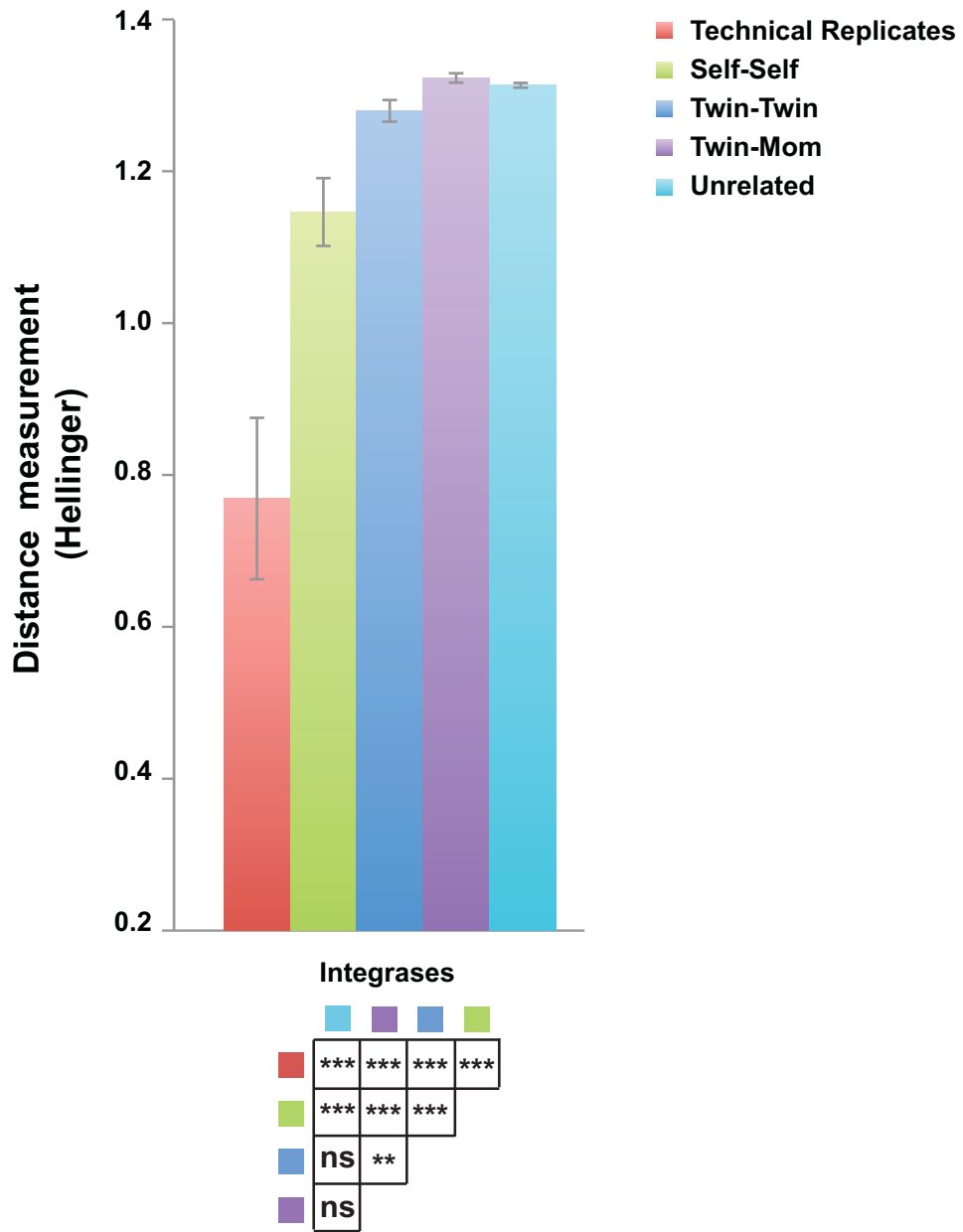
Multiple alignment of the indicated viral protein (highlighted in red) with all proteins from 121 human gut microbial genomes that harbored the same domain or motif was performed using Muscle<sup>19</sup>. Approximate maximum likelihood trees were generated using FastTree<sup>20</sup>. Bars represent the number of amino acid substitutions per position.

Reyes *et al.*, Supplementary Fig. 12



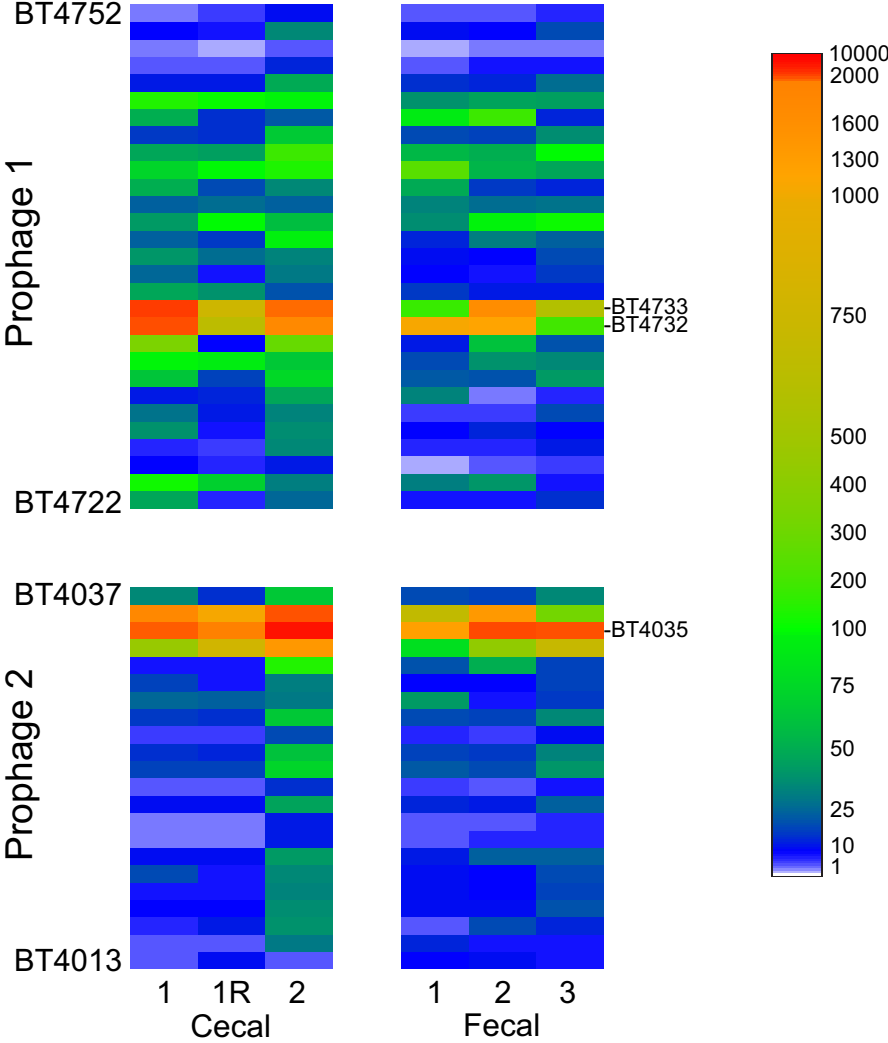
**Fig. S13. Sequence diversity of integrase genes in VLP viromes.** The number of pyrosequencer reads in each VLP sample with significant hits to known integrases present in the NR\_Viral\_DB and in prophages found in 121 human gut microbial genomes were identified and used to generate a distance matrix. Average distances among technical replicates (two shotgun datasets produced from a given VLP DNA preparation), among samples obtained from the same individual over time (intrapersonal variation), and samples obtained from co-twins, twins and their mothers or unrelated individuals, are graphed (mean  $\pm$  s.e.m). The significance of differences between the groups was calculated using Student's t-test. \*\*\*  $p < 0.001$ ; \*\*  $p < 0.01$ , ns,  $p > 0.05$ .

Reyes *et al.*, Supplementary Fig. 13



**Fig. S14. Normalized RNA-Seq counts for predicted prophages in *Bacteroides thetaiotaomicron* VPI-5482.** RNA-Seq was performed using rRNA-depleted RNA samples prepared from cecal and fecal contents harvested from gnotobiotic mice co-colonized for 2 weeks with *B. thetaiotaomicron* and *M. formatexigens* (n=3 animals). Expression levels are shown for each ORF (see color key for normalized read counts; normalization based on sequencing effort and length of each predicted ORF). Active expression is defined as a normalized read count >100. This strain of *B. thetaiotaomicron* contains two prophages. One of the prophages (labeled 1) contains a linked pair of highly expressed ORFs encoding an Xre family anti-toxin (BT4733) and a putative toxin (BT4732) while the other prophage contains a cluster of three highly expressed genes [two hypothetical proteins flanking a Xre family anti-toxin (BT4035)].

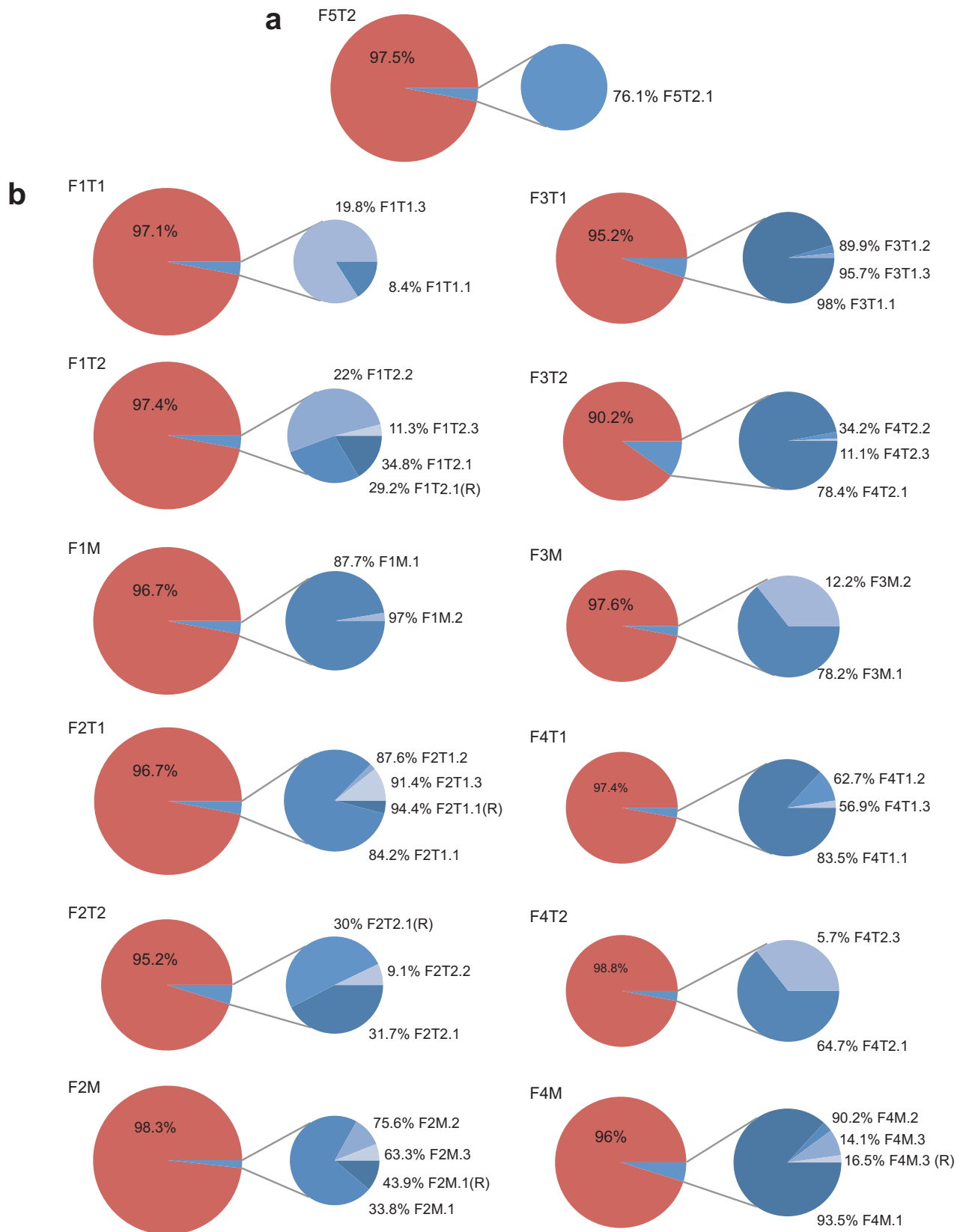
Reyes *et al.*, Supplementary Fig. 14



**Fig. S15. Representation of VLP pyrosequencer reads in fecal microbiomes and vice versa.** The percentage of reads from fecal microbiomes with significant similarity to VLP-derived reads (blastn, e-value  $<1e-7$ ) is represented as a blue wedge within the red pie charts. This wedge is expanded to the right in the form a second blue pie chart that shows the percentage of reads from each of the different time point VLP preparations that have significant similarity with reads from the fecal microbiome from time point 1. (a) The percentage of shared reads between the deeply sequenced F5T2 VLP preparation and corresponding deeply sequenced fecal microbiome (293,654 and 2,579,680 reads, respectively). (b) Data derived from shallowly sequenced fecal viromes and microbiomes.



Reyes *et al.*, Supplementary Fig. 15



## Supplementary Tables

**Table S1. Sequencing effort for VLP preparations from 32 fecal samples obtained from 4 sets of MZ twins and their mothers.** Technical replicates were performed on 6 DNA samples involving independent whole genome amplification and shotgun 454 FLX pyrosequencing. Sample F5T2.1 was subjected to deeper sequencing. NA, a fecal specimen was not available in sufficient quantity to purify VLPs at this time point.

**Table S2. Sequencing effort for bacterial 16S rRNA genes present in the fecal microbiota of study participants.**

**Table S3. Shotgun sequencing effort for fecal community DNA (microbiome) samples.**

**Table S4. CD-hit cluster-based alpha diversity metrics.**

**Table S5. PHACCS-based alpha diversity metrics.**

**Table S6. Matrix of VLP samples x reference human microbial gut genomes where significant coverage to prophages in the microbial host was identified.** (a) Percent of the prophage genome covered by reads from a given VLP sample. (b) Fold coverage per bp of the prophage genome, normalized to 10,000 reads. Yellow highlights instances where the prophage was covered over more than 50% of its length.

**Table S7. Matrix of VLP samples x the 88 large contigs assembled from the aggregate VLP dataset showing (a) the percentage of the contig covered by reads from a given VLP sample and (b) fold-coverage per bp of each contig.** Data are

normalized by randomly mapping 14,000 reads per VLP sample. Yellow highlights instances where a given contig has  $\geq 50\%$  coverage with reads from a given VLP virome.

**Table S8. Contig x VLP sample matrix of contigs present in more than one VLP sample.** The percent identity between VLP-pyrosequencer reads and the corresponding contig is shown. Dashes indicate that no reads corresponding to the contig were present in the VLP sample (threshold; minimum of 80% overlap with the contig over the length of the read)

**Table S9. List of 121 sequenced human gut-derived microbial genomes used for generating a reference list of KEGG second level pathways and COG assignments.** The presence or absence of CRISPRs in the genomes of the 74 organisms used to search for these elements is noted.

**Table S10. List of 396 sequenced microbial genomes used to identify prophage sequences for the NR\_Viral\_DB.**

**Table S11. The number of VLP reads with similarity over more than 90% of their length to CRISPR spacers present in either the fecal microbiome of the same individual or in a reference gut-associated microbial genome.** Counts are normalized (10,000 reads per sample). The bottom row shows the number of spacers identified in each fecal microbiome sample (see *Supplementary Discussion* for further definition of the criteria used to select spacers from the fecal microbiome datasets to query VLP datasets).

**Table S1. Shotgun pyrosequencing of DNA purified from fecal VLPs**

**Number of reads per dataset**

Family	Family Member	Time.1	Time.2	Time.3
F1	T1	23,284	NA	43,609
	T2	43,350	31,045	28,044
	M	48,769	24,498	NA
F2	T1	71,432	40,414	26,634
	T2	40,932	36,319	NA
	M	58,379	27,647	35,561
F3	T1	18,578	19,866	30,441
	T2	53,410	33,807	28,922
	M	25,098	37,697	NA
F4	T1	24,563	20,674	14,483
	T2	27,937	NA	30,013
	M	24,980	23,731	30,207
F5	T2	48,432		

**Replicates**

F4	M.3	16,081
F1	T2.1	30,141
F2	T1.1	19,506
F2	T2.1	41,719
F2	M.1	34,012
F5	T2.1	245,222

**Number of nucleotides per dataset**

Family	Family Member	Time.1	Time.2	Time.3
F1	T1	5,480,138	NA	10,439,191
	T2	10,319,498	7,278,429	6,663,475
	M	11,874,381	6,013,335	NA
F2	T1	17,244,379	9,845,469	6,560,103
	T2	9,684,954	8,812,248	NA
	M	14,173,440	6,637,882	8,597,871
F3	T1	4,487,018	4,788,497	7,333,512
	T2	12,609,532	8,164,157	6,950,693
	M	6,019,033	9,106,849	NA
F4	T1	5,949,161	4,919,740	3,437,755
	T2	6,772,788	NA	7,115,420
	M	5,934,901	5,652,431	7,365,500
F5	T2	11,712,401		

**Replicates**

F4	M.3	3,931,490
F1	T2.1	7,360,504
F2	T1.1	4,747,264
F2	T2.1	10,056,492
F2	M.1	8,297,597
F5	T2.1	58,444,932

**Table S2. Pyrosequencing effort for 16S rRNA V2 region amplicons**

**Number of reads per dataset**

Family	Family Member	Time.1	Time.2	Time.3
F1	T1	6,415	1,627	40,583
	T2	15,495	1,957	2,074
	M	7,870	1,799	2,816
F2	T1	9,343	2,886	3,030
	T2	13,991	3,606	2,562
	M	7,717	4,325	3,350
F3	T1	9,837	3,953	10,392
	T2	19,586	5,045	2,417
	M	15,294	4,752	30,294
F4	T1	11,936	4,220	1,588
	T2	12,672	4,603	1,856
	M	13,789	3,284	3,071

**Table S3. Shotgun pyrosequencing effort for fecal community DNA (microbiome) samples**

**Number of reads per dataset**

Family	Family Member	Time.1
F1	T1	217,386
	T2	443,640
	M	510,972
F2	T1	414,754
	T2	490,776
	M	535,763
F3	T1	498,880
	T2	495,040
	M	413,772
F4	T1	519,072
	T2	549,700
	M	434,187
F5	T2	2,579,680

**Number of nucleotides per dataset**

Family	Family Member	Time.1
F1	T1	51,926,180
	T2	79,297,532
	M	103,228,389
F2	T1	95,417,867
	T2	101,090,755
	M	118,742,924
F3	T1	82,616,445
	T2	98,548,138
	M	89,199,789
F4	T1	92,506,950
	T2	112,549,303
	M	81,764,398
F5	T2	910,456,203

**Table S4. CD-hit cluster-based alpha diversity metrics**

		Sample	Cluster Shannon Index	Expected #Clusters	Average Genome Size	Expected #Virotypes
Family 1	Co-twin 1	1	10.94	56327	5594	403
		3	13.39	653728	34025	769
		1	11.59	108486	11863	366
	Co-twin 2	1(R)	12.24	207752	14533	572
		2	13.64	838359	12091	2773
		3	12.31	221107	19716	449
	Mother	1	12.66	315416	73725	171
2		11.22	74731	42095	71	
Family 2	Co-twin 1	1	12.00	163342	30437	215
		1(R)	11.72	122634	49931	98
		2	11.98	160020	43526	147
		3	11.91	149282	47792	125
	Co-twin 2	1	13.09	482461	9908	1948
		1(R)	13.43	682963	15585	1753
		2	12.56	285882	7552	1514
	Mother	1	13.13	503089	32162	626
		1(R)	13.22	552748	38326	577
		2	12.66	315897	49478	255
		3	12.83	374537	32373	463
Family 3	Co-twin 1	1	11.11	66702	51239	52
		2	11.27	78619	31767	99
		3	11.02	60812	43052	57
	Co-twin 2	1	13.19	536799	43499	494
		2	12.32	224460	30704	292
		3	13.60	803043	20416	1573
	Mother	1	11.82	136453	36091	151
		2	12.07	174413	27692	252
Family 4	Co-twin 1	1	12.52	274276	28033	391
		2	11.71	121210	26193	185
		3	11.66	115724	39954	116
	Co-twin 2	1	12.47	259988	31832	327
		3	11.71	121545	45812	106
		1	12.73	338213	14954	905
	Mother	2	12.22	202101	27135	298
		3	12.62	304012	31133	391
		3(R)	12.15	188697	29101	259
Family 5	Co-twin 2	1	13.49	725374	33678	862
		1(R)	13.85	1034661	33940	1219

**Table S5. PHACCS-based alpha diversity metrics**

		Sample	Shannon Index	Evenness	Richness
Family 1	Co-twin 1	1	3.72	0.90	62
		3	4.22	0.87	131
		1	3.68	0.91	60
	Co-twin 2	2	5.24	0.83	536
		3	3.37	0.94	37
		1	3.82	0.69	245
Mother	2	4.09	0.66	490	
Family 2	Co-twin 1	1	2.19	0.98	10
		2	2.28	0.97	11
		3	2.99	0.84	127
	Co-twin 2	1	4.51	0.92	138
		2	4.07	0.95	71
		1	3.57	0.92	50
	Mother	2	2.71	0.95	18
		3	2.85	0.95	20
Family 3	Co-twin 1	1	2.29	0.97	11
		2	2.46	0.97	13
		3	3.46	0.78	984
	Co-twin 2	1	3.72	0.85	78
		2	3.02	0.92	28
		3	4.25	0.92	102
	Mother	1	2.84	0.96	19
		2	2.93	0.96	21
Family 4	Co-twin 1	1	3.31	0.94	34
		2	3.34	0.94	35
		3	2.62	0.92	18
	Co-twin 2	1	2.83	0.96	19
		3	2.61	0.96	15
		1	3.40	0.97	33
	Mother	2	3.18	0.97	27
		3	3.23	0.91	36











Table S8. Percent similarity between reads in VLP samples and 88 large viral contigs

Sample	Family 1						Family 2						Family 3						Family 4					
	Co-twin 1		Co-twin 2		Mother		Co-twin 1		Co-twin 2		Mother		Co-twin 1		Co-twin 2		Mother		Co-twin 1		Co-twin 2		Mother	
	1	3	1	2	3	1	2	1	2	3	1	2	3	1	2	3	1	2	1	2	3	1	2	3
Contig_255	-	-	99.75	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Contig_381	-	-	99.81	99.78	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Contig_389	-	-	99.85	99.82	99.41	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Contig_396	-	-	99.77	99.77	99.53	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Contig_378	-	-	99.81	99.79	99.66	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Contig_384	-	-	99.86	99.80	99.93	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Contig_1233	-	-	99.82	99.82	99.83	-	-	88.16	87.96	88.03	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Contig_20922	-	-	99.83	99.81	99.83	-	-	88.09	88.06	88.05	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Contig_20743	-	-	-	-	-	99.84	-	-	-	-	-	-	-	-	-	-	-	-	-	-	92.87	-	-	-
Contig_424	-	-	-	-	-	99.79	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Contig_2194	-	-	-	-	-	99.84	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	86.32
Contig_22692	-	-	-	-	-	-	99.86	-	-	99.88	-	-	-	-	-	-	-	-	-	-	-	-	-	86.75
Contig_21166	-	-	-	-	-	-	-	99.67	98.95	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Contig_2613	-	-	-	-	-	-	-	98.02	99.04	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Contig_21891	-	-	-	-	-	-	-	99.41	99.29	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Contig_21357	-	-	-	-	-	-	-	99.80	99.69	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Contig_20560	-	-	-	-	-	-	-	99.70	99.74	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Contig_2618	-	-	-	-	-	-	-	99.84	99.77	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Contig_3634	-	-	-	-	-	-	-	99.48	99.80	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Contig_1567	-	-	-	-	-	-	-	-	-	86.67	86.58	86.54	-	-	-	-	-	-	-	-	-	-	-	-
Contig_1550	-	-	-	-	-	-	-	-	-	87.81	87.99	87.64	-	-	-	-	-	-	-	-	-	-	-	-
Contig_19925	-	-	-	-	-	-	-	-	-	99.82	99.79	99.78	-	-	-	-	-	-	-	-	-	-	-	-
Contig_2285	-	-	-	-	-	-	-	-	-	99.93	100.00	99.88	-	-	-	-	-	-	-	-	-	-	-	-
Contig_228	-	-	-	-	-	-	-	-	-	99.95	-	99.94	-	-	-	-	-	-	-	-	-	-	-	-
Contig_22223	-	-	-	-	-	-	-	-	-	99.92	99.74	99.95	-	-	-	-	-	-	-	-	-	-	-	-
Contig_2090	-	-	-	-	-	-	-	-	-	-	-	-	99.88	99.85	-	-	-	-	-	-	-	-	-	-
Contig_2244	-	-	-	-	-	-	-	-	-	-	-	-	99.82	99.83	99.82	-	-	-	-	-	-	-	-	-
Contig_291	-	-	-	-	-	-	-	-	-	-	-	-	99.82	99.81	99.84	-	-	-	-	-	-	-	-	-
Contig_2061	-	-	-	-	-	-	-	-	-	-	-	-	99.83	99.85	99.85	-	-	-	-	-	-	-	-	-
Contig_20697	-	-	-	-	-	-	-	-	-	-	-	-	99.78	99.88	99.87	-	-	-	-	-	-	-	-	-
Contig_2058	-	-	-	-	-	-	-	-	-	-	-	-	99.70	99.81	99.94	-	-	-	-	-	-	-	-	-
Contig_1567	-	-	-	-	-	-	-	-	-	-	-	-	87.30	-	-	99.81	-	-	-	-	-	-	86.71	-
Contig_1550	-	-	-	-	-	-	-	-	-	86.58	86.54	-	-	-	-	99.83	-	-	-	-	-	-	87.89	-
Contig_1603	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	99.76	99.73	-	-
Contig_423	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	99.71	99.73	-	-
Contig_22976	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	99.73	99.74	-	-
Contig_405	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	99.77	99.78	-	-
Contig_406	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	99.78	99.78	-	-
Contig_22975	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	99.77	99.81	-	-
Contig_2788	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	99.83	99.78
Contig_22597	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	99.81	99.80
Contig_2786	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	99.83	99.80

**Table S9. List of 121 reference human gut-associated microbial genomes**

<b>Species and strain designation</b>	<b>GenBank Accession number</b>	<b>CRISPR Loci</b>
Actinomyces odontolyticus	NZ_AAYI00000000	Present
Alistipes putredinis	NZ_ABFK00000000	Absent
Anaerococcus hydrogenalis	NZ_ABXA00000000	Present
Anaerofustis stercorihominis	NZ_ABIL00000000	Absent
Anaerostipes caccae	NZ_ABAX00000000	Present
Anaerotruncus colihominis	NZ_ABGD00000000	Absent
Bacteroides caccae ATCC 43185	NZ_AAVM00000000	Absent
Bacteroides capillosus	NZ_AAXG00000000	Present
Bacteroides cellulosilyticus	NZ_ACCH00000000	
Bacteroides coprocola	NZ_ABIY00000000	Present
Bacteroides coprophilus	NZ_ACBW00000000	
Bacteroides dorei	NZ_ABWZ00000000	Present
Bacteroides eggerthii	NZ_ABVO00000000	Absent
Bacteroides finegoldii	NZ_ABXI00000000	Absent
Bacteroides fragilis 3 1 12	NZ_ABZX00000000	Present
Bacteroides fragilis NCTC 9343	NC_006347	
Bacteroides fragilis YCH46	NC_003228	
Bacteroides intestinalis	NZ_ABJL00000000	Absent
Bacteroides ovatus ATCC 8483	NZ_AAXF00000000	Absent
Bacteroides plebeius	NZ_ABQC00000000	Present
Bacteroides sp 1 1 6	NZ_ACIC00000000	
Bacteroides sp. D1	NZ_ACAB00000000	
Bacteroides sp. D2	NZ_ACGA00000000	
Bacteroides stercoris	NZ_ABFZ00000000	Absent
Bacteroides thetaiotaomicron 7330		
Bacteroides thetaiotaomicron VPI-5482	NC_004663	Absent
Bacteroides uniformis ATCC 8492	NZ_AAYH00000000	Absent
Bacteroides vulgatus ATCC 8482	NC_009614	Absent
Bacteroides WH2		
Bacteroides xylanisolvens XB1A	ProjectID:39177	Absent
Bifidobacterium adolescentis	NZ_AAXD00000000	Present
Bifidobacterium adolescentis ATCC 15703	NC_008618	Present
Bifidobacterium angulatum	NZ_ABYS00000000	Present
Bifidobacterium animalis HN019.fa	NZ_ABOT00000000	
Bifidobacterium animalis subsp. lactis AD011	NC_011740	
Bifidobacterium breve	NZ_ACCG00000000	Absent
Bifidobacterium catenulatum	NZ_ABXY00000000	Present
Bifidobacterium dentium	NZ_ABIX00000000	Present
Bifidobacterium gallicum	NZ_ABXB00000000	Present
Bifidobacterium longum DJO10A	NC_010816	Present
Bifidobacterium longum NCC2705	NC_004307	
Bifidobacterium pseudocatenulatum	NZ_ABXX00000000	Present
Blautia hansenii	NZ_ABYU00000000	Present
Blautia hydrogenotrophica DSM 10507	NZ_ACBZ00000000	Absent
Bryantella formatexigens DSM 14469	NZ_ACCL00000000	
Butyrivibrio crossotus	NZ_ABWN00000000	Absent
Catenibacterium mitsuokai	NZ_ACCK00000000	
Citrobacter sp	NZ_ACDJ00000000	
Clostridium asparagiforme	NZ_ACCJ00000000	
Clostridium bartlettii	NZ_ABEZ00000000	Present
Clostridium bolteae	NZ_ABCC00000000	Present
Clostridium hiranonis	NZ_ABWP00000000	Present
Clostridium hylemonae	NZ_ABYI00000000	
Clostridium leptum	NZ_ABCB00000000	Absent
Clostridium methylpentosum	NZ_ACEC00000000	
Clostridium nexile	NZ_ABWO00000000	Present
Clostridium ramosum	NZ_ABFX00000000	Present
Clostridium scindens ATCC 35704	NZ_ABFY00000000	Present
Clostridium sp L2	NZ_AAYW00000000	Present
Clostridium sp M62 1	NZ_ACFX00000000	

Clostridium sp SS2	NZ_ABGC00000000	
Clostridium spiroforme DSM 1552	NZ_ABIK00000000	Present
Clostridium sporogenes	NZ_ABKW00000000	Present
Clostridium symbiosum	ProjectID:18183	Present
Collinsella aerofaciens ATCC 25986	NZ_AAVN00000000	Absent
Collinsella intestinalis	NZ_ABXH00000000	Absent
Collinsella stercoris	NZ_ABXJ00000000	Absent
Coprococcus comes	NZ_ABVR00000000	
Coprococcus eutactus	NZ_ABEY00000000	Present
Desulfovibrio piger ATCC29098	NZ_ABXU00000000	Present
Desulfovibrio piger GOR1	ProjectID:30377	
Dorea formicigenerans	NZ_AAXA00000000	Absent
Dorea longicatena DSM 13814	NZ_AAXB00000000	Present
Enterobacter cancerogenus	NZ_ABWM00000000	Present
Escherichia coli str. K-12 substr. MG1655	NC_000913	
Escherichia fergusonii ATCC 35469	NC_011835	
Eubacterium bifforme	NZ_ABYT00000000	Present
Eubacterium dolichum	NZ_ABAW00000000	Present
Eubacterium eligens ATCC 27750	NC_012778	Present
Eubacterium hallii	NZ_ACEP00000000	Present
Eubacterium rectale ATCC 33656	NC_012781	Present
Eubacterium ventriosum	NZ_AAVL00000000	Present
Faecalibacterium prausnitzii M21/2	NZ_ABED00000000	Present
Fusobacterium sp. 4 1 13	NZ_ACDE00000000	
Fusobacterium varium ATCC27725	NZ_ACIE00000000	
Helicobacter pylori HPAG1	NC_008086	
Holdemania filiformis	NZ_ACCF00000000	
Lactobacillus casei ATCC 334	NC_008526	
Lactobacillus delbrueckii subsp. bulgaricus ATCC 11842	NC_008054	
Lactococcus lactis subsp. cremoris MG1363	NC_009004	
Lactococcus lactis subsp. cremoris SK11	NC_008527	
Lactococcus lactis subsp. lactis II1403	NC_002662	
M23A		
Methanobrevibacter smithii ATCC 35061	NC_009515	Present
Methanobrevibacter smithii DSM2374	NZ_ABYV00000000	
Methanobrevibacter smithii DSM2375	NZ_ABYW00000000	
Methanosphaera stadtmanae DSM 3091	NC_007681	
Mitsuokella multacida	NZ_ABWK00000000	Present
Parabacteroides distasonis ATCC 8503	NC_009615	Present
Parabacteroides johnsonii	NZ_ABYH00000000	Absent
Parabacteroides merdae	NZ_AAXE00000000	Present
Peptostreptococcus micros	NZ_ABEE00000000	Present
Prevotella copri	NZ_ACBX00000000	Absent
Proteus penneri	NZ_ABVP00000000	
Providencia alcalifaciens	NZ_ABXW00000000	Absent
Providencia rettgeri	NZ_ACCI00000000	
Providencia rustigianii	NZ_ABXV00000000	Present
Providencia stuartii	NZ_ABJD00000000	Present
Roseburia intestinalis L1	NZ_ABYJ00000000	
Ruminococcus bromiiL263	ProjectID:39153	Absent
Ruminococcus gnavus	NZ_AAYG00000000	Present
Ruminococcus lactaris	NZ_ABOU00000000	Present
Ruminococcus obeum ATCC 29174	NZ_AAVO00000000	Absent
Ruminococcus torques ATCC 27756	NZ_AAVP00000000	Absent
Shigella sp. D9	NZ_ACDL00000000	
Streptococcus infantarius	NZ_ABJK00000000	Present
Streptococcus thermophilus CNRZ1066	NC_006448	
Streptococcus thermophilus DN001147.fa	NC_006449	
Streptococcus thermophilus LMD-9	NC_008532	
Subdoligranulum variabile	NZ_ACBY00000000	
Victivallis vadensis ATCC BAA-548	NZ_ABDE00000000	

**Table S10. List of 396 microbial genomes used to search for prophages**

Species and strain designation	GenBank Accession No	Species and strain designation	GenBank Accession No
Acinetobacter sp. ADP1	NZ_005966	Legionella pneumophila subsp. pneumophila str. Philadelphia	NC_002942
Actinomyces odontolyticus	NZ_AAY100000000	Leifsonia xylis subsp. xylis str. CTCB07	NC_006087
Agrobacterium tumefaciens str. C58	NC_003063	Leptospira interrogans serovar Copenhageni str. Fiocruz L1-	NC_005823
Agrobacterium tumefaciens str. C58	NC_003062	Leptospira interrogans serovar Copenhageni str. Fiocruz L1-	NC_005824
Alistipes putredinis	NZ_ABFK000000000	Leptospira interrogans serovar Lai str. 56601	NC_004342
Anabaena variabilis ATCC 29413	NC_007413	Leptospira interrogans serovar Lai str. 56601	NC_004343
Anaerococcus hydrogenalis	NZ_ABXA000000000	Listeria innocua Clj11262	NC_003212
Anaerofustis stercorihominis	NZ_ABIL000000000	Listeria monocytogenes EGD-e	NC_003210
Anaerostipes caccae	NZ_ABAX000000000	Listeria monocytogenes str. 4b F2365	NC_002973
Anaerotruncus colihominis	NZ_ABGD000000000	M23A	
Anaplasma marginale str. St. Maries	NC_004842	Magnetospirillum magneticum AMB-1	NC_007626
Aquifex aeolicus VFS	NC_000918	Mannheimia succiniciproducens MBEL55E	NC_006300
Aster yellows witches'-broom phytoplasma AYWB	NC_007716	Mesoplasma florum L1	NC_006055
Azoarcus sp. EbN1	NC_006513	Mesorhizobium loti MAFF303099	NC_002678
Bacillus anthracis str. 'Ames Ancestor'	NC_007530	Methanobrevibacter smithii ATCC 35061	NC_009515
Bacillus anthracis str. Ames	NC_003997	Methanobrevibacter smithii DSM2374	NZ_ABYV000000000
Bacillus anthracis str. Sterne	NC_005945	Methanobrevibacter smithii DSM2375	NZ_ABYW000000000
Bacillus cereus ATCC 10987	NC_003909	Methanospaera stadmanae DSM 3091	NC_007681
Bacillus cereus ATCC 14579	NC_004722	Methylococcus capsulatus str. Bath	NC_002977
Bacillus cereus E33L	NC_006274	Mitsuokella multacida	NZ_ABWK000000000
Bacillus clausii KSM-K16	NC_006582	Moorella thermoacetica ATCC 39073	NC_007644
Bacillus halodurans C-125	NC_002570	Mycobacterium avium subsp. paratuberculosis str. k10	NC_002944
Bacillus licheniformis ATCC 14580	NC_006270	Mycobacterium bovis AF2122/97	NC_002945
Bacillus subtilis subsp. subtilis str. 168	NC_000964	Mycobacterium leprae TN	NC_002677
Bacillus thuringiensis serovar konkukian str. 97-27	NC_005957	Mycobacterium tuberculosis CDC1551	NC_002755
Bacteroides caccae ATCC 43185	NZ_AAVM000000000	Mycobacterium tuberculosis H37Rv	NC_009662
Bacteroides capillosus	NZ_AAXG000000000	Mycoplasma capricolum subsp. capricolum ATCC 27343	NC_007633
Bacteroides cellulolyticus	NZ_ACCH000000000	Mycoplasma gallisepticum R	NC_004829
Bacteroides coprocola	NZ_ABYI000000000	Mycoplasma genitalium G-37	NC_000908
Bacteroides coprophilus	NZ_ACBW000000000	Mycoplasma hyopneumoniae 232	NC_006360
Bacteroides dorei	NZ_ABWZ000000000	Mycoplasma hyopneumoniae 7448	NC_007332
Bacteroides eggerthii	NZ_ABVO000000000	Mycoplasma hyopneumoniae J	NC_007295
Bacteroides finegoldii	NZ_ABXI000000000	Mycoplasma mobile 163K	NC_006908
Bacteroides fragilis NCTC 9343	NC_003228	Mycoplasma mycoides subsp. mycoides SC str. PG1	NC_005364
Bacteroides fragilis YCH46	NC_006347	Mycoplasma penetrans HF-2	NC_004432
Bacteroides intestinalis	NZ_ABJL000000000	Mycoplasma pneumoniae M129	NC_000912
Bacteroides ovatus ATCC 8483	NZ_AAXF000000000	Mycoplasma pulmonis UAB CTIP	NC_002771
Bacteroides plebeius	NZ_ABQC000000000	Mycoplasma synoviae 53	NC_007294
Bacteroides stercoris	NZ_ABFZ000000000	Neisseria gonorrhoeae FA 1090	NC_002946
Bacteroides thetaiotaomicron VPI-5482	NC_004663	Neisseria meningitidis MC58	NC_003112
Bacteroides uniformis ATCC 8492	NZ_AAYH000000000	Neisseria meningitidis Z2491	NC_003116
Bacteroides vulgatus ATCC 8482	NC_009614	Nitrobacter winogradskyi Nb-255	NC_007406
Bartonella henselae str. Houston-1	NC_005956	Nitrosococcus oceani ATCC 19707	NC_007484
Bartonella quintana str. Toulouse	NC_005955	Nitrosomonas europaea ATCC 19718	NC_004757
Bdellovibrio bacteriovorus HD100	NC_005363	Nitrosospora multiformis ATCC 25196	NC_007614
Bifidobacterium adolescentis	NZ_AAXD000000000	Nocardia farcinica IFM 10152	NC_006361
Bifidobacterium adolescentis ATCC 15703	NC_008618	Nostoc sp. PCC 7120	NC_003272
Bifidobacterium angulatum	NZ_ABSY000000000	Novosphingobium aromaticivorans DSM 12444	NC_007794
Bifidobacterium breve	NZ_ACCG000000000	Oceanobacillus iheyensis HTE831	NC_004193
Bifidobacterium catenulatum	NZ_ABXV000000000	Onion yellows phytoplasma OY-M	NC_005303
Bifidobacterium dentium	NZ_ABXI000000000	Parabacteroides distans ATCC 8503	NC_009615
Bifidobacterium gallium	NZ_ABXB000000000	Parabacteroides johnsonii	NZ_ABYH000000000
Bifidobacterium longum DJO10A	NC_010816	Parabacteroides merdae	NZ_AAXE000000000
Bifidobacterium longum NCC2705	NC_004307	Parachlamydia sp. UWE25	NC_005861
Bifidobacterium pseudocatenulatum	NZ_ABXX000000000	Pasteurella multocida subsp. multocida str. Pm70	NC_002663
Blautia hansenii	NZ_ABYU000000000	Pelobacter carbinolicus DSM 2380	NC_007498
Blautia hydrogenotrophica DSM 10507	NZ_ACBZ000000000	Peloidictyon luteolum DSM 273	NC_007512
Bordetella pertussis Tohama I	NC_002929	Peptostreptococcus micros	NZ_ABEEO00000000
Borrelia burgdorferi B31	NC_001318	Photobacterium profundum SS9	NC_006370
Borrelia garinii PBI	NC_006156	Photobacterium profundum SS9	NC_006371
Bradyrhizobium japonicum USDA 110	NC_004463	Phorhydradus luminescens subsp. laumondii TTO1	NC_005126
Brucella abortus biovar 1 str. 9-941	NC_006932	Phytophthora ramorum str. 9803	NC_002950
Brucella abortus biovar 1 str. 9-941	NC_006933	Prevotella copri	NZ_ACBX000000000
Brucella melitensis 16M	NC_003317	Prochlorococcus marinus str. MIT 9312	NC_007577
Brucella melitensis 16M	NC_003318	Prochlorococcus marinus str. MIT 9313	NC_005071
Brucella melitensis biovar Abortus	NC_007618	Prochlorococcus marinus str. NATL2A	NC_007335
Brucella suis 1330	NC_004310	Prochlorococcus marinus subsp. marinus str. CCMP1375	NC_005042
Brucella suis 1330	NC_004311	Prochlorococcus marinus subsp. pastoris str. CCMP1986	NC_005072
Bryantella formatexigens DSM 14469	NZ_AACL000000000	Propionibacterium acnes KPA171202	NC_006085
Buchnera aphidicola str. APS (Acyrthosiphon pisum)	NC_002528	Proteus penneri	NZ_ABP000000000
Buchnera aphidicola str. Bp (Baizongia pistaciae)	NC_004545	Providencia alcalifaciens	NZ_ABXW000000000
Buchnera aphidicola str. Sg (Schizaphis graminum)	NC_004061	Providencia rettgeri	NZ_ACCI000000000
Burkholderia mallei ATCC 23344	NC_006348	Providencia rustigianii	NZ_ABXV000000000
Burkholderia mallei ATCC 23344	NC_006349	Providencia stuartii	NZ_ABDJ000000000
Burkholderia pseudomallei 1710b	NC_007434	Pseudoalteromonas haloplanktis TAC125	NC_007481
Burkholderia pseudomallei 1710b	NC_007435	Pseudoalteromonas haloplanktis TAC125	NC_007482
Burkholderia pseudomallei K96243	NC_006350	Pseudomonas aeruginosa PAO1	NC_002516
Burkholderia pseudomallei K96243	NC_006351	Pseudomonas fluorescens Pf-5	NC_004129
Burkholderia sp. 383	NC_007509	Pseudomonas fluorescens PfO-1	NC_007492
Burkholderia sp. 383	NC_007510	Pseudomonas putida KT2440	NC_002947
Burkholderia sp. 383	NC_007511	Pseudomonas syringae pv. phaseolicola 1448A	NC_005773
Burkholderia thailandensis E264	NC_007650	Pseudomonas syringae pv. syringae B728a	NC_007005
Burkholderia thailandensis E264	NC_007651	Pseudomonas syringae pv. tomato str. DC3000	NC_004578
Butyrivibrio crossotus	NZ_ABWN000000000	Psychrobacter arcticus 273-4	NC_007204
Campylobacter jejuni RM1221	NC_003912	Ralstonia eutropha JMP134	NC_007347
Campylobacter jejuni subsp. jejuni NCTC 11168	NC_002163	Ralstonia eutropha JMP134	NC_007348
Candidatus Blochmannia floridanus	NC_005061	Ralstonia solanacearum GMI1000	NC_003295
Candidatus Blochmannia pennsylvanicus str. BPEN	NC_007292	Rhodobacter sphaeroides 2.4.1	NC_007493
Candidatus Pelagibacter ubique HTCC1062	NC_007205	Rhodobacter sphaeroides 2.4.1	NC_007494
Carboxydotherrmus hydrogenoformans Z-2901	NC_007503	Rhodopirellula baltica SH 1	NC_005027
Catenibacterium mitsuokai	NZ_ACKK000000000	Rhodopseudomonas palustris CGA009	NC_005296
Caulobacter crescentus CB15	NC_002696	Rhodopseudomonas palustris HaA2	NC_007778
Chlamydia muridarum Nigg	NC_002620	Rhodospirillum rubrum ATCC 11170	NC_007643
Chlamydia trachomatis A/HAR-13	NC_007429	Rickettsia conorii str. Malish 7	NC_003103



Chlamydia trachomatis D/UW-3/CX	NC_000117	Rickettsia felis URRWXCal2	NC_007109
Chlamydia abortus S26/3	NC_004552	Rickettsia prowazekii str. Madrid E	NC_000963
Chlamydia caviae GPIC	NC_003361	Rickettsia typhi str. Wilmington	NC_006142
Chlamydia pneumoniae AR39	NC_002179	Roseburia intestinalis L1	NZ_ABYJ00000000
Chlamydia pneumoniae CWL029	NC_000922	Ruminococcus gnavus	NZ_AAYG00000000
Chlamydia pneumoniae J138	NC_002491	Ruminococcus lactaris	NZ_ABOU00000000
Chlamydia pneumoniae TW-183	NC_005043	Ruminococcus obeum ATCC 29174	NZ_AAVO00000000
Chlorobium chlorochromatii CaD3	NC_007514	Ruminococcus torques ATCC 27756	NZ_AAVP00000000
Chlorobium tepidum TLS	NC_002932	Salinibacter ruber DSM 13855	NC_007677
Chromobacterium violaceum ATCC 12472	NC_005085	Salmonella enterica subsp. enterica serovar Choleraesuis str	NC_006905
Citrobacter sp	NZ_ACDJ000000000	Salmonella enterica subsp. enterica serovar Paratyphi A str	NC_006511
Clostridium acetobutylicum ATCC 824	NC_003030	Salmonella enterica subsp. enterica serovar Typhi str. CT18	NC_003198
Clostridium asparagiforme	NZ_ACCJ000000000	Salmonella enterica subsp. enterica serovar Typhi Ty2	NC_004631
Clostridium bartlettii	NZ_ABEZ000000000	Salmonella typhimurium LT2	NC_003197
Clostridium bolteae	NZ_ABCC000000000	Shewanella oneidensis MR-1	NC_004347
Clostridium hiranonis	NZ_ABWP000000000	Shigella boydii Sb227	NC_007613
Clostridium hylemonae	NZ_ABYI000000000	Shigella dysenteriae Sd197	NC_007606
Clostridium leptum	NZ_ABCB000000000	Shigella flexneri 2a str. 2457T	NC_004741
Clostridium methylpentosum	NZ_ACEC000000000	Shigella flexneri 2a str. 301	NC_004337
Clostridium nexile	NZ_ABWQ000000000	Shigella sonnei Ss046	NC_007384
Clostridium perfringens str. 13	NC_003366	Silicibacter pomeroyi DSS-3	NC_003911
Clostridium ramosum	NZ_ABFX000000000	Sinorhizobium meliloti 1021	NC_003047
Clostridium scindens ATCC 35704	NZ_ABFY000000000	Sodalis glossinidius str. 'morsitans'	NC_007712
Clostridium sp L2	NZ_AAYW000000000	Staphylococcus aureus RF122	NC_007622
Clostridium sp M62 1	NZ_ACFX000000000	Staphylococcus aureus subsp. aureus COL	NC_002951
Clostridium sp SS2	NZ_ABGC000000000	Staphylococcus aureus subsp. aureus MRSA252	NC_002952
Clostridium spiroforme DSM 1552	NZ_ABIK000000000	Staphylococcus aureus subsp. aureus MSSA476	NC_002953
Clostridium sporogenes	NZ_ABKW000000000	Staphylococcus aureus subsp. aureus Mu50	NC_002758
Clostridium symbiosum	ProjectID:18183	Staphylococcus aureus subsp. aureus MW2	NC_003923
Clostridium tetani E88	NC_004557	Staphylococcus aureus subsp. aureus N315	NC_002745
Collinsella aerofaciens ATCC 25986	NZ_AAVN000000000	Staphylococcus aureus subsp. aureus NCTC 8325	NC_007795
Collinsella intestinalis	NZ_ABXH000000000	Staphylococcus aureus subsp. aureus USA300	NC_007793
Collinsella stercoris	NZ_ABXJ000000000	Staphylococcus epidermidis ATCC 12228	NC_004461
Colwellia psychrerythraea 34H	NC_003910	Staphylococcus epidermidis RP62A	NC_002976
Coprococcus comes	NZ_ABVR000000000	Staphylococcus haemolyticus JCSC1435	NC_007168
Coprococcus eutactus	NZ_ABEY000000000	Staphylococcus saprophyticus subsp. saprophyticus ATCC 1530	NC_007350
Corynebacterium diphtheriae NCTC 13129	NC_002935	Streptococcus agalactiae 2603V/R	NC_004116
Corynebacterium efficiens YS-314	NC_004369	Streptococcus agalactiae A909	NC_007432
Corynebacterium glutamicum ATCC 13032	NC_006958	Streptococcus agalactiae NEM316	NC_004368
Corynebacterium jeikeium K411	NC_007164	Streptococcus infantarius	NZ_ABJK000000000
Coxiella burnetii RSA 493	NC_002971	Streptococcus mutans UA159	NC_004350
Cyanobacteria bacterium Yellowstone A-Prime	NC_007775	Streptococcus pneumoniae R6	NC_003098
Cyanobacteria bacterium Yellowstone B-Prime	NC_007776	Streptococcus pneumoniae TIGR4	NC_003028
Dechloromonas aromatica RCB	NC_007298	Streptococcus pyogenes M1 GAS	NC_002737
Dehalococcoides ethenogenes 195	NC_002936	Streptococcus pyogenes MGAS10394	NC_006086
Dehalococcoides sp. CBD81	NC_007356	Streptococcus pyogenes MGAS315	NC_004070
Deinococcus radiodurans R1	NC_001263	Streptococcus pyogenes MGAS5005	NC_007297
Deinococcus radiodurans R1	NC_001264	Streptococcus pyogenes MGAS6180	NC_007296
Desulfotalea psychrophila LSV54	NC_006138	Streptococcus pyogenes MGAS8232	NC_003485
Desulfovibrio desulfuricans G20	NC_007519	Streptococcus pyogenes SSI-1	NC_004606
Desulfovibrio piger ATCC29098	NZ_ABXU000000000	Streptococcus thermophilus CNRZ1066	NC_006449
Desulfovibrio vulgaris subsp. vulgaris str. Hildenborough	NC_002937	Streptococcus thermophilus LMG 18311	NC_006448
Dorea formicigenerans	NZ_AAXA000000000	Streptomyces avermitilis MA-4680	NC_003155
Dorea longicatena DSM 13814	NZ_AAXB000000000	Streptomyces coelicolor A3(2)	NC_003888
Ehrlichia canis str. Jake	NC_007354	Subdoligranulum variabile	NZ_ACBY000000000
Ehrlichia ruminantium str. Gardel	NC_006831	Symbiobacterium thermophilum IAM 14863	NC_006177
Ehrlichia ruminantium str. Welgevonden	NC_005295	Synechococcus elongatus PCC 6301	NC_006576
Ehrlichia ruminantium str. Welgevonden	NC_006832	Synechococcus elongatus PCC 7942	NC_007604
Enterobacter cancerogenus	NZ_ABWM000000000	Synechococcus sp. CC9605	NC_007516
Enterococcus faecalis V583	NC_004668	Synechococcus sp. CC9902	NC_007513
Erwinia carotovora subsp. atroseptica SCRI1043	NC_004547	Synechococcus sp. WH 8102	NC_005070
Erythrobacter litoralis HTCC2594	NC_007722	Synechocystis sp. PCC 6803	NC_000911
Escherichia coli CFT073	NC_004431	Syntrophus aciditrophicus SB	NC_007759
Escherichia coli K12	NC_000913	Thermoanaerobacter tengcongensis MB4	NC_003869
Escherichia coli O157:H7	NC_002695	Thermobifida fusca YX	NC_007333
Escherichia coli O157:H7 EDL933	NC_002655	Thermosynechococcus elongatus BP-1	NC_004113
Eubacterium bifforme	NZ_ABYT000000000	Thermotoga maritima MSB8	NC_000853
Eubacterium dolichum	NZ_ABAW000000000	Thermus thermophilus HB27	NC_005835
Eubacterium hallii	NZ_ACEP000000000	Thermus thermophilus HB8	NC_006461
Eubacterium ventriosum	NZ_AAVL000000000	Thiobacillus denitrificans ATCC 25259	NC_007404
Faecalibacterium prausnitzii M21/2	NZ_ABED000000000	Thiomicrospira crunigena XCL-2	NC_007520
Francisella tularensis subsp. tularensis SCHU 54	NC_006570	Thiomicrospira denitrificans ATCC 33889	NC_007575
Frankia sp. Cc13	NC_007777	Treponema denticola ATCC 35405	NC_002967
Fusobacterium nucleatum subsp. nucleatum ATCC 25586	NC_003454	Treponema pallidum subsp. pallidum str. Nichols	NC_000919
Geobacillus kaustophilus HTA426	NC_006510	Tropheryma whipplei str. Twist	NC_004572
Geobacter metallireducens GS-15	NC_007517	Tropheryma whipplei TW08/27	NC_004551
Geobacter sulfurreducens PCA	NC_002939	Ureaplasma parvum serovar 3 str. ATCC 700970	NC_002162
Gloeobacter violaceus PCC 7421	NC_005125	Vibrio cholerae O1 biovar eltor str. N16961	NC_002505
Gluconobacter oxydans 621H	NC_006677	Vibrio cholerae O1 biovar eltor str. N16961	NC_002506
Haemophilus ducreyi 35000HP	NC_002940	Vibrio fischeri ES114	NC_006840
Haemophilus influenzae 86-028NP	NC_007146	Vibrio fischeri ES114	NC_006841
Haemophilus influenzae Rd KW20	NC_000907	Vibrio parahaemolyticus RIMD 2210633	NC_004603
Hahella chejuensis KCTC 2396	NC_007645	Vibrio parahaemolyticus RIMD 2210633	NC_004605
Helicobacter hepaticus ATCC 51449	NC_004917	Vibrio vulnificus CMCP6	NC_004459
Helicobacter pylori 1039kx1	ProjectID:40515	Vibrio vulnificus CMCP6	NC_004460
Helicobacter pylori 1039kx2	ProjectID:40519	Vibrio vulnificus YJ016	NC_005139
Helicobacter pylori 26695	NC_000915	Vibrio vulnificus YJ016	NC_005140
Helicobacter pylori 345kx1	ProjectID:40545	Wigglesworthia glossinidia endosymbiont of Glossina brevipa	NC_004344
Helicobacter pylori 345kx2	ProjectID:40547	Wolbachia endosymbiont of Drosophila melanogaster	NC_002978
Helicobacter pylori 98_10	NZ_ABSX000000000	Wolbachia endosymbiont strain TRS of Brugia malayi	NC_006833
Helicobacter pylori B128	NZ_ABSY000000000	Xanthomonas axonopodis pv. citri str. 306	NC_005090
Helicobacter pylori G27	NC_011333	Xanthomonas campestris pv. campestris str. 8004	NC_003919
Helicobacter pylori HPAG1	NC_008086	Xanthomonas campestris pv. campestris str. ATCC 33913	NC_007086
Helicobacter pylori J99	NC_000921	Xanthomonas campestris pv. vesicatoria str. 85-10	NC_003902
Helicobacter pylori P12	NC_011498	Xanthomonas oryzae pv. oryzae KACC10331	NC_007508
Holdemanella filiformis	NZ_ACCF000000000	Xanthomonas oryzae pv. oryzae MAFF 311018	NC_006834
Idiomarina loihiensis L2TR	NC_006512		NC_007705

Lactobacillus acidophilus NCFM  
Lactobacillus johnsonii NCC 533  
Lactobacillus plantarum WCFS1  
Lactobacillus sakei subsp. sakei 23K  
Lactococcus lactis subsp. lactis II1403  
Legionella pneumophila str. Lens  
Legionella pneumophila str. Paris

NC\_006814  
NC\_005362  
NC\_004567  
NC\_007576  
NC\_002662  
NC\_006369  
NC\_006368

Xylella fastidiosa 9a5c  
Xylella fastidiosa Temecula1  
Yersinia pestis biovar Medievalis str. 91001  
Yersinia pestis CO92  
Yersinia pestis KIM  
Yersinia pseudotuberculosis IP 32953  
Zymomonas mobilis subsp. mobilis ZM4

NC\_002488  
NC\_004556  
NC\_005810  
NC\_003143  
NC\_004088  
NC\_006155  
NC\_006526

**Table S11. Number of VLP reads with similarity over more than 90% of their length to CRISPR spacers present in either the fecal microbiome of the same individual or a reference human gut-associated microbial genome**

		Family 1			Family 2			Family 3			Family 4			Family 5	Ref Gut Genomes
		Co-twin 1	Co-twin 2	Mother	Co-twin 1	Co-twin 2	Mother	Co-twin 1	Co-twin 2	Mother	Co-twin 1	Co-twin 2	Mother	Co-twin 2	
Family 1	Co-twin 1	1	-	-	-	-	-	-	-	-	-	-	-	-	8.16
		3	-	-	-	-	-	-	-	-	-	-	-	0.23	0.69
	Co-twin 2	1	-	-	-	-	-	-	-	-	-	-	-	3.65	66.35
		1(R)	-	-	-	-	-	-	-	-	-	-	-	7.38	80.05
		2	-	-	-	-	-	-	-	-	-	-	-	-	65.07
	Mother	3	-	-	-	-	-	-	-	-	-	-	-	-	1.78
1		-	-	-	-	-	-	-	-	-	-	-	-	0.41	
	2	-	-	-	-	-	-	-	-	-	-	-	-	-	
Family 2	Co-twin 1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
		1(R)	-	-	-	-	-	0.42	-	-	-	-	-	-	3.78
	Co-twin 2	2	-	-	-	-	-	-	-	-	-	-	-	-	4.45
		3	-	-	-	-	-	-	-	-	-	-	-	-	-
		1	-	-	-	-	-	-	-	-	-	-	-	8.39	0.24
	Co-twin 2	1(R)	-	-	-	-	-	-	-	-	-	-	-	5.62	-
2		-	-	-	-	-	-	-	-	-	-	-	3.03	1.93	
Mother	1	-	-	-	-	-	-	-	-	-	-	-	-	0.29	
	1(R)	-	-	-	-	-	-	-	-	-	-	-	1.03	0.34	
	2	-	-	-	-	-	-	-	-	-	-	-	-	0.36	
	3	-	-	-	-	-	-	-	-	-	-	-	-	-	
Family 3	Co-twin 1	1	-	-	-	-	-	-	-	-	-	-	-	0.54	-
		2	-	-	-	-	-	-	-	-	-	-	-	-	-
		3	-	-	-	-	-	-	-	-	-	-	-	-	-
	Co-twin 2	1	-	-	-	0.94	-	-	-	-	-	-	-	-	2.81
		2	-	-	-	-	-	-	-	-	-	-	-	-	0.59
		3	-	-	-	-	-	-	-	-	-	-	-	-	-
Mother	1	-	-	-	-	-	-	-	-	-	-	-	-	7.17	
	2	-	-	-	-	-	-	0.53	-	-	-	-	0.80	4.51	
Family 4	Co-twin 1	1	-	-	-	-	-	-	-	-	-	-	-	2.04	6.11
		2	-	-	-	-	-	-	-	-	-	-	-	0.48	9.19
		3	-	-	-	-	-	-	-	-	-	-	-	-	-
	Co-twin 2	1	-	-	-	-	-	-	-	-	-	-	-	8.23	46.18
		3	-	-	-	-	-	-	-	-	-	-	-	-	-
		1	-	-	-	-	-	-	-	-	-	-	-	-	0.40
Mother	2	-	-	-	-	-	-	-	-	-	-	-	-	-	
	3	-	-	-	-	-	-	-	-	-	-	-	-	-	
	3(R)	-	-	-	-	-	-	-	-	-	-	-	-	-	
Family 5	Co-twin 2	1	-	-	-	-	-	-	-	-	-	-	2.68	0.21	
	1(R)	-	-	-	-	-	-	-	-	-	-	-	3.56	1.23	

**No. of spacers per fecal microbiome**

**9      24      52      13      36      17      26      14      22      21      57      49      241      2196**