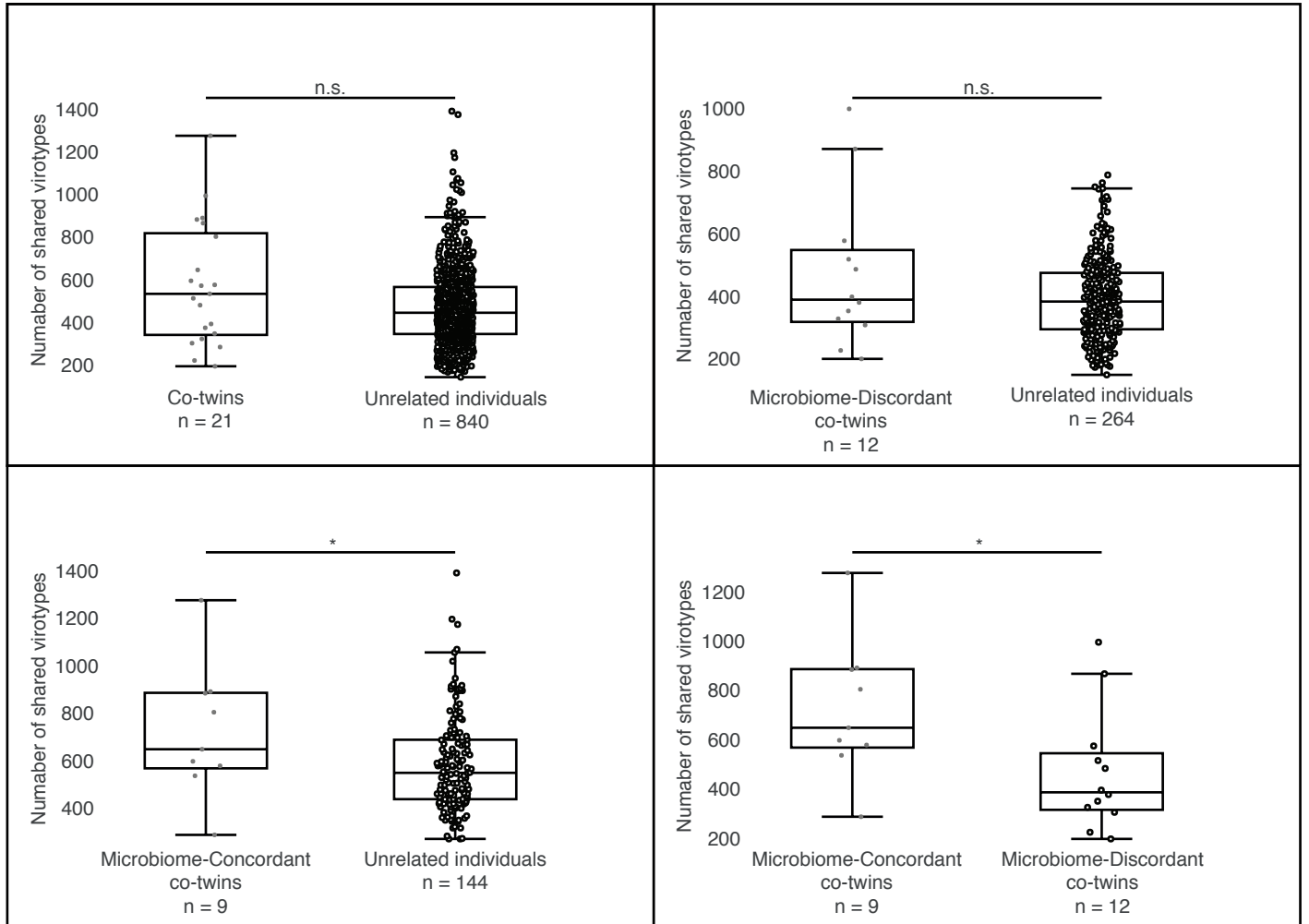
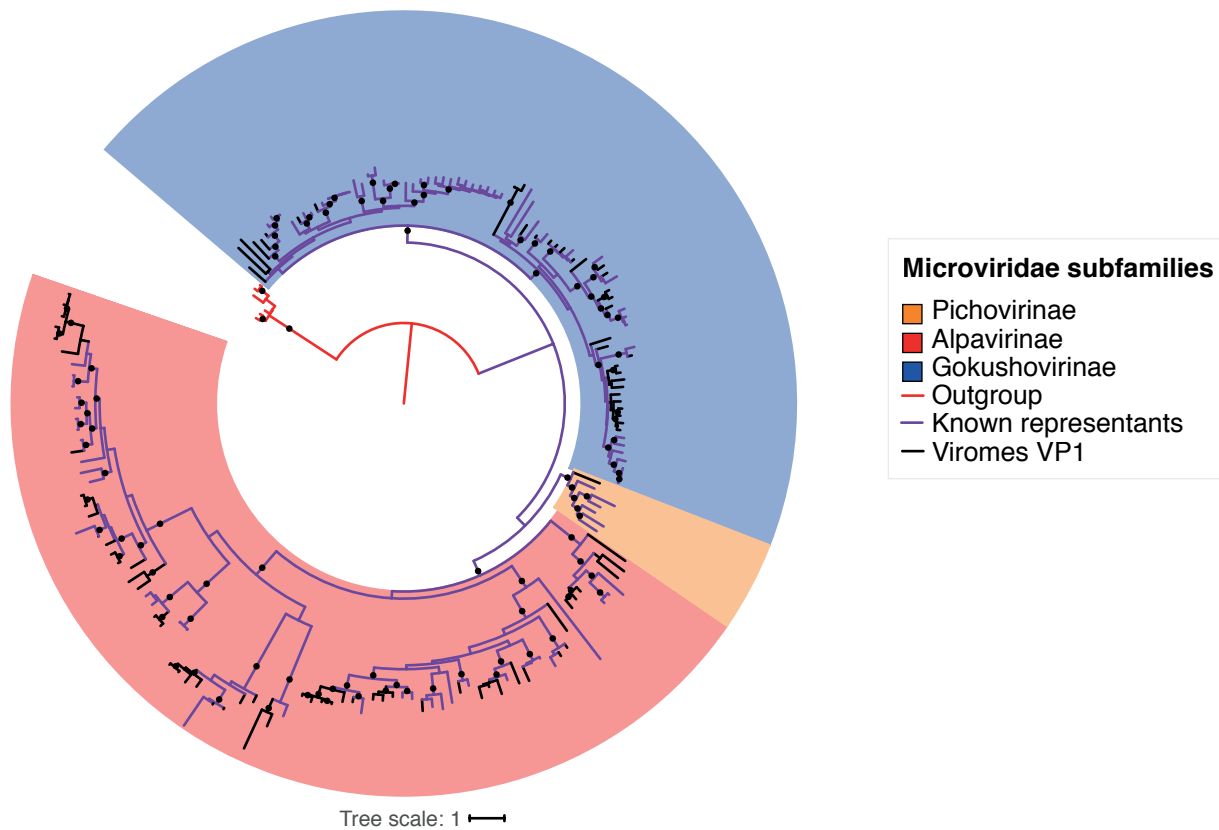
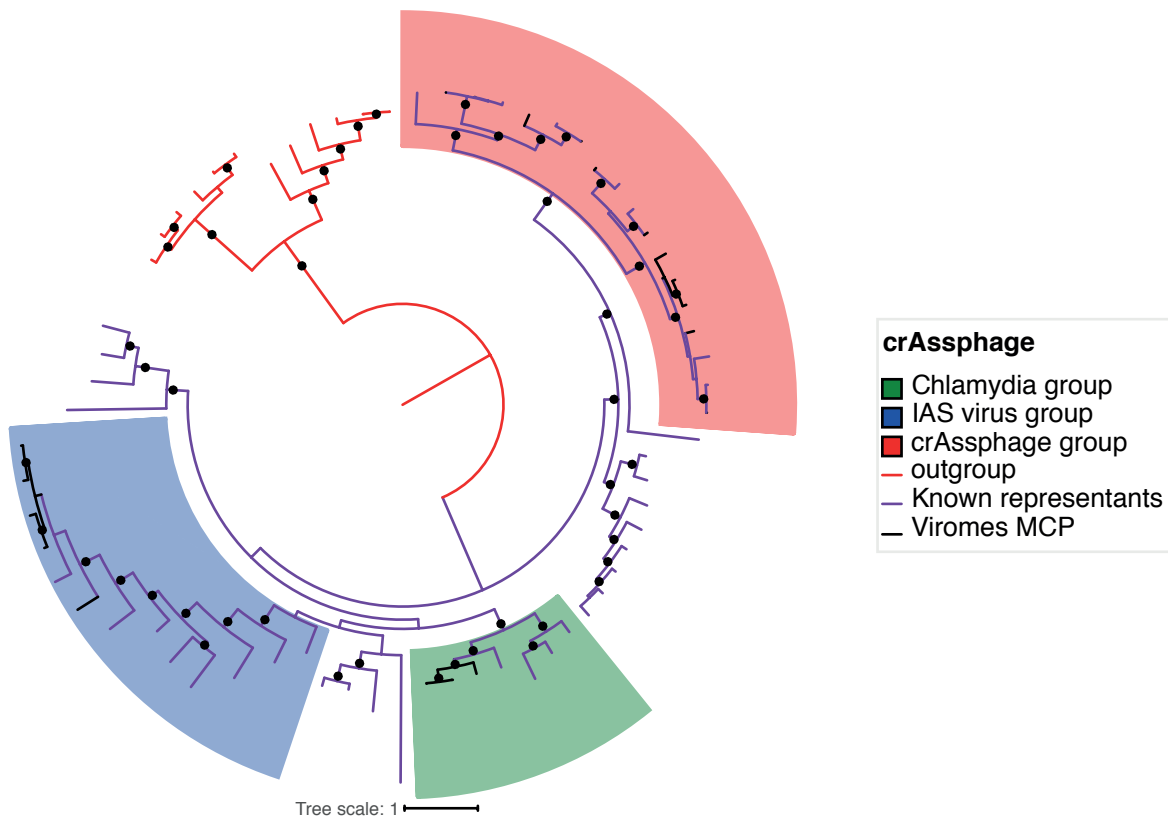


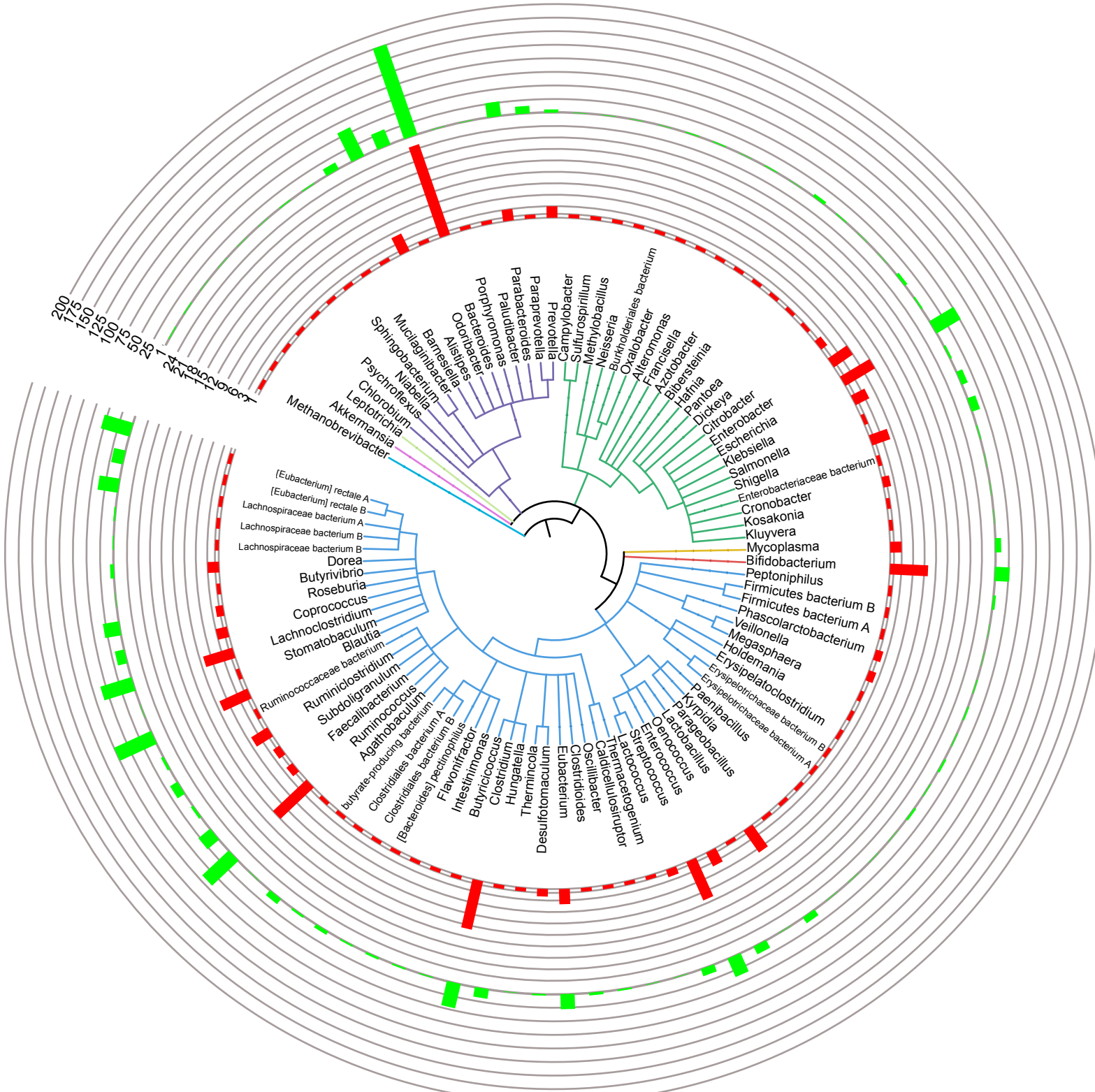
**Figure S1. Related to Figure 1.** Schematic representation summarizing the procedures applied to (left) the “large-insert-size library” and (right) the “short-insert-size library” to obtain three different layers of information used to analyze the virome diversity of the microbiome-concordant and microbiome-discordant co-twins.



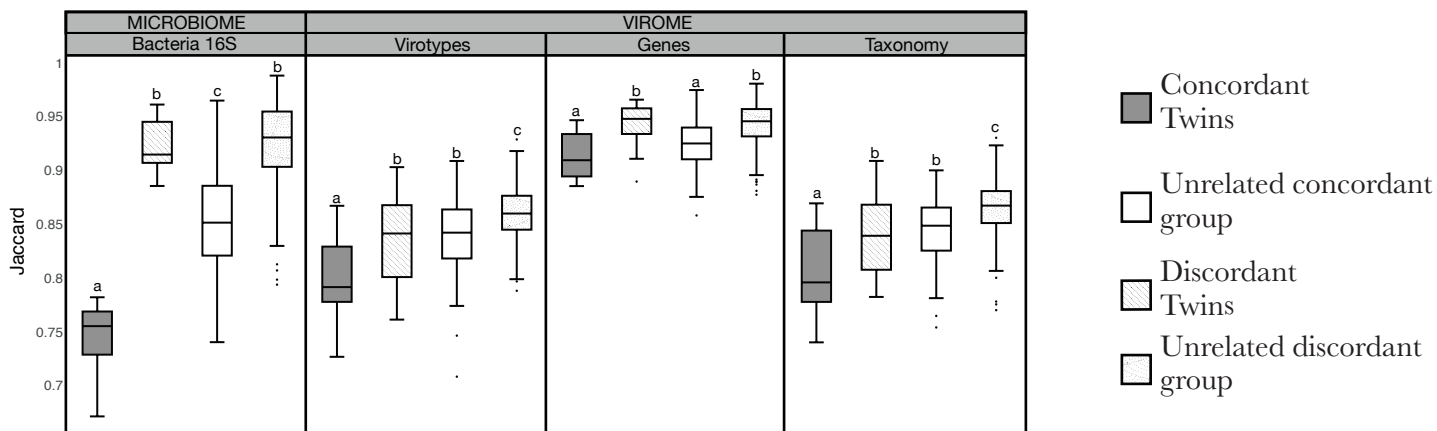
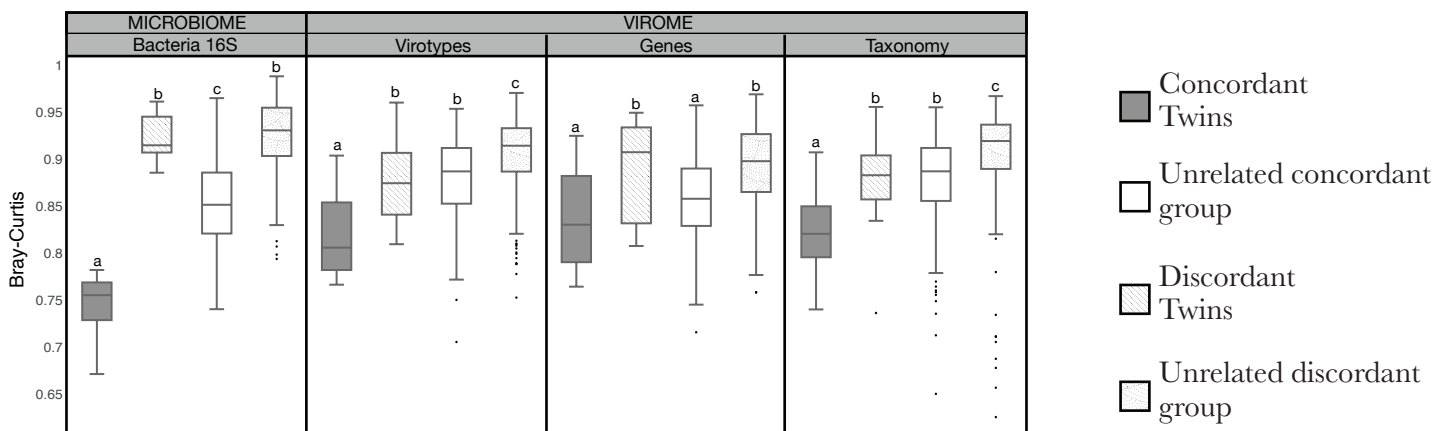
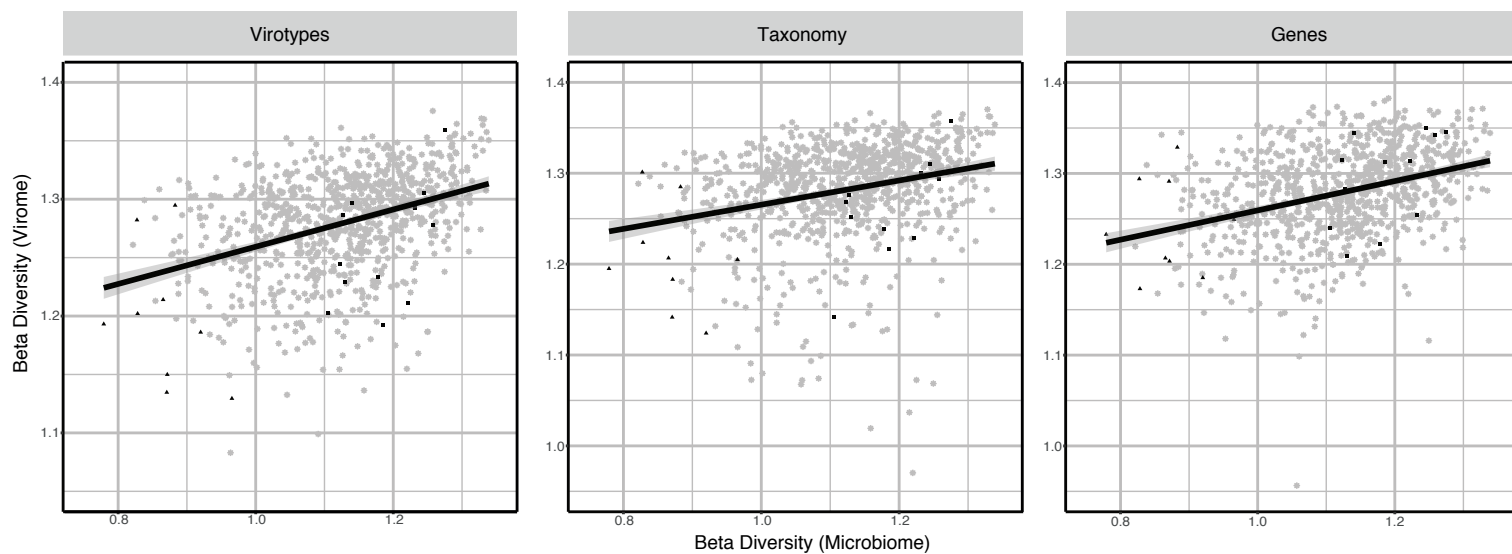
**Figure S2. Related to Figure 4.** Box plots showing the distribution of the number of shared virotypes between different groups made from the 21 MZ co-twins. (Upper left) All co-twins vs unrelated individuals. (Upper right) Microbiome-discordant co-twins vs unrelated individuals in the same group. (Lower left) Microbiome-concordant co-twins vs unrelated individuals in the same group. (Lower right) Microbiome-concordant co-twins vs microbiome-discordant co-twins. Mann-Whitney's U test. \*  $p < 0.05$ ; n.s: no significant difference.

**A****B**

**Figure S3. Related to Figure 4.** Maximum likelihood phylogenetic analysis of (A) the VP1 protein of *Microviridae* phages and (B) the MCP protein of crAssphage found in the 42 MZ viromes. Reference sequences are in purple, outgroup sequences are in red while the different MCP or VP1 proteins found in this work are labeled in black. Circles in the nodes indicate bootstrap values above 70%. Scale: Average substitutions per site.



**Figure S4. Related to STAR Methods.** Phage-host interaction prediction. Cladogram based on the NCBI taxonomy showing the bacteria identified as hosts. The cladogram is summarized by genus, and clades are colored by Phylum. Blue: Firmicutes; Red: Actinobacteria; Yellow: Tenericutes; Green: Proteobacteria; Purple: Bacteroidetes; Light green: Fusobacteriia; Magenta: Verrucomicrobia; Light blue: Euryarchaeota. Red bars indicate the number of species in each genus, and green bars show the dereplicated number of contigs associated to each genus (i.e., if a contig was found associated to two species in that genus, it is only shown one time).

**A****B****C**

**Figure S5. Related to Figure 5 and Figure 6.** Box plots showing the distribution of (A) the Jaccard distances and (B) Bray-Curtis distances for microbiomes and viromes, according to the three different layers of information recovered (virotypes, genes and taxonomy). Significant differences between means (Mann-Whitney's U test) are denoted with different letters. Groups and n values as in Figure 6. (C) Correlation between virome  $\beta$ -diversity and microbiome  $\beta$ -diversity ( $n=840$ ). Virotypes: Pearson correlation coefficient among all individuals = 0.382 ( $p = 0.0005$ , Mantel test),  $m = 0.167$ ,  $p = 0$ ,  $R^2 = 0.157$ ; Pearson correlation coefficient among co-twins = 0.522,  $m = 0.188$ ,  $p = 0.015$ ,  $R^2 = 0.1508$ ; Taxonomy annotated contigs: Pearson correlation coefficient among all individuals = 0.266 ( $p = 0.003$ , Mantel test),  $m = 0.140$ ,  $p = 0$ ,  $R^2 = 0.0796$ ; Pearson correlation coefficient among co-twins = 0.512,  $m = 0.186$ ,  $p = 0.017$ ,  $R^2 = 0.224$ ; Genes: Pearson correlation coefficient among all individuals = 0.344 ( $p = 0.0009$ , Mantel test),  $m = 0.162$ ,  $p = 0$ ,  $R^2 = 0.123$ ; Pearson correlation coefficient among co-twins = 0.53,  $m = 0.182$ ,  $p = 0.012$ ,  $R^2 = 0.248$ . Lines describe linear regressions of pairwise distances among all individuals. Triangles indicate concordant-microbiome co-twins and squares indicate discordant-microbiome co-twins.