

The importance of the FGT virome

The female genital tract (FGT) microbiome is highly dynamic, with a unique ecology that exists as distinct community state types (CSTs) across time and between women. FGT microbiome CSTs, classified into 5 types based on dominance of certain Lactobacillus species (I, II, III, V) or dominance of non-Lactobacillus bacteria (CST IV), are strongly associated with women's and infant health. The FGT virome has been understudied relative to non-viral microbes, due to the great diversity of viral biology, their intractability in most experimental settings, and limited computational and experimental methods. However, FGT virome is critical for host and bacterial interactions that determine immune and health phenotypes. We thus provide the first comprehensive characterization of the FGT virome integrating 1) two US cohorts with paired, longitudinal metagenomic and metatranscriptomic FGT samples, totalling 80 subjects, and 2) non-Western cohorts.



• MetaPhIAn profiled a total of 812 unique non-viral species and BAQLaVa profiled 781 viral species (VGBs).

• 90, 28 and 66	52 VGBs with eukaryotic,
prokaryotic and u	unknown host, respectively.
VGB_68755 -	Lactobacillus_iners -
VGB_108116 -	Lactobacillus_crispatus -
VGB_126315	Gardnerella_vaginalis -
VGB_543 -	Lactobacillus_jensenii
VGB_51587	Fannyhessea_vaginae
VGB_118896	Megasphaera_lornae -
VGB_18517	Lactobacillus_gasseri
VGB_37414 -	Prevotella_amnii -
VGB_9638 -	Prevotella_bivia -
VGB_29953 -	Coriobacteriales_sp.
0% 25% 50% 75%	0% 20% 40% 60% 80%
mean_abundance prevalence	e mean_abundance prevalence

Boston Children's Defining the Female Genital Tract Virome Hospital

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try		Μ	GX	N	ΜΤΧ		
		200		183			
		16	62	111			
ade	sh	4	12	0			
ia		29	91	0			
		1065		294			
Ш	III		IV		V		
5	19	34			5		
0	12	3 63			15		
0	80	120)	9		
5	22	2 217		,	29		
Sample reads KneadData							
bacterial depletion							
BAQLaVa							
MetaPhIAn							
IVIAASLIN3							

CST IV has a distinct virome

- Ordination analysis of bacterial profiles shows clustering of individual CSTs with inter-CST transition densities.
- perpendicularly from a mix of other CSTs. This suggests unique viruses in CST IV while other CSTs likely share most viruses.



CST IV associates with diverse viruses

MaAsLin3 was used to test for association of variables of metadata CST, country and ethnicity with VGB abundance and prevalence.

- The majority of the associations are based on prevalence indicating ecosystem diversity.
- Consistent with the ordination above most of the associations were between VGBs and CST IV followed by Zambia.
- But most of viral space profiled by BAQLaVa is novel and not yet well annotated/characterized.
- are over 50 • There papillomavirus VGBs but only one has significant associations.

(-Inf,-1.5] (-1.5,-0.75] (-0.75,0] (0.75,1.5] (1.5,Inf)

• In contrast, ordination of viral profiles has CST IV extending

Prevalence Abundance VGB_48055 [.] VGB_20760 -VGB_37414 -VGB_49250 -VGB_29477 -Caudoviricetes -VGB_84737 VGB_44200 -VGB_543 -→ VGB_118896 -VGB_13350 -VGB_82992 -VGB_20 -Caudoviricetes VGB_119089 -VGB_108116-Caudoviricetes Caudoviricetes -Caudoviricetes -Caudoviricetes Caudoviricetes VGB_34 -VGB_18517 Alphapapillomavi Beta coefficient N N N N Covariates P_{FDR}



with (BD) VGBs as that

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