Descriptive patterns of vaginal phage-bacterial host dynamics in pregnant women

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Prokaryote-infecting viruses (bacteriophages) are known to impact gut microbial communities through interactions with their bacterial hosts. In the female genital tract (FGT), there is an abundance of both lytic (virulent) and temperate bacteriophages integrated as prophages into bacterial genomes. These possibly play important roles in reproductive health. However, interactions between phages and their vaginal bacterial hosts remain under-characterized. Here, we sequenced bacterial DNA from the FGT of South African pregnant women and used a bioinformatics approach to identify phage sequences and predict their lifestyle and host interactions.

DNA was extracted from vaginal swabs collected from pregnant women at 24 - 35 weeks gestation, and shotgun sequenced on Illumina NovaSeq 6000 (2x150bp). Contigs were assembled using SPAdes, and viral-like contigs (>1000nts) were identified using geNomad and BLASTn with the NCBI Viral Genome database. Contigs were clustered at 98% similarity with CD-HIT to represent variant viral operational taxonomic units (vOTUs). Putative bacterial hosts and bacteriophage lifestyles were predicted using iPHoP and PhaBOX respectively.

Prophages identified were predominantly Caudoviricetes with some microviruses. Predicted bacterial hosts included *Lactobacillus*, *Gardnerella,* and *Prevotella* species. In some cases, the same phage vOTUs were found in multiple species, suggesting a generalist pattern. Most Caudoviricetes vOTUs predicted to infect *Lactobacillus* were linked to multiple *Lactobacillus* species. However, several vOTUs were predicted to infect only *L. iners,* which accounted for majority of *Lactobacillus* host predictions. Interestingly, a single vOTU with stigmata of lytic lifestyle was predicted to have broad host specificity across the *Lactobacillus* genus, including *L. crispatus.* In contrast, a wider range of vOTUs was predicted to infect vaginal dysbiosis-associated bacteria, including *Prevotella* and *Gardnerella* species, with both temperate and lytic predicted lifestyles. These genera were also among the most abundant in the bacterial taxonomic profiles, suggesting that phage-host predictions may be influenced by bacterial abundance.

Although our analysis was limited to qualitative predictions, these preliminary findings suggest that the vaginal virome has genus-specific phage-host dynamics. Further research is needed to identify, characterize, and quantify vaginal phage vOTUs in a larger cohort of women, validate these predicted phage-host interactions, and assess their implications in reproductive health.