

MICROBIOTA

Bacteriophage diversity in the urinary microbiome

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New research, published in the *Journal of Bacteriology*, has revealed the diversity of the lysogenic bacteriophage population within the urinary microbiome. Furthermore, differences in the abundance of bacteriophages were observed between bacteria isolated from women with lower urinary tract symptoms (LUTS) and those without, suggesting that bacteriophages could affect urinary health.

Bacteriophages are important in microbial communities; however, research on the urinary microbiome has mainly focused on its bacterial components. Previous analysis of the genomes of bacteria isolated from the bladder revealed unique bacteriophage sequences, prompting Miller-Ensminger and colleagues to investigate further.

These researchers hypothesized that urinary microbiota contain a large prophage population, based on the observation that lysogenic bacteriophages outnumber obligately lytic bacteriophages in gut microbiota. To explore this hypothesis, the investigators examined 181 bacterial isolates from women with or without LUTS for the presence of bacteriophage sequences. The VirSorter tool was used to detect bacteriophage sequences existing as an extrachromosomal plasmid (categories 1–3) and those that were integrated into the bacterial chromosome (categories 4–6). High-confidence predictions of bacteriophage sequences could be made for categories 1, 2, 4, and 5, whereas lower-confidence sequence predictions were made for categories 3 and 6.

Overall, 226 high-confidence and 231 lower-confidence bacteriophage sequences were identified. “We found that latent bacteriophages are abundant in these urinary bacteria, with some bacterial isolates harbouring 10 different bacteriophage sequences,” Catherine Putonti, corresponding author, tells *Nature Reviews Urology*. “In total, 86% of the genomes examined, which represent the phylogenetic diversity of bacteria found within the bladder, had one or more phage sequences.” Genome size showed only a low correlation with the number of bacteriophage sequences within the genome, and no significant difference was found between the average length

of bacterial genomes containing bacteriophage sequences and those lacking them.

Of the 226 sequences predicted with high confidence, 38% showed similar prophage sequences to those observed in previously sequenced genomes. “Most (57%) of the latent bacteriophages identified in this study are novel — they exhibit no sequence similarity to known phage sequences,” explains Putonti. Furthermore, the majority of sequences predicted with lower confidence also seemed to be novel (61%).

“As the genomes in our study were isolated from healthy women as well as women with LUTS (such as urinary tract infection, urge urinary incontinence, and stress urinary incontinence), we then were interested to see if there was any correspondence between the number of bacteriophages found and the reported symptom (or lack thereof),” continues Putonti. “Notably, this investigation was not our initial intention of the study; nevertheless, we identified some quite intriguing associations.” For example, a common Actinomycetaceae bacteriophage was found in isolates from women with overactive bladder; this phage was not found in any of the Actinomycetaceae isolated from asymptomatic women.

“These observations certainly raise the question of whether bacteriophages have a role in urinary health or symptoms,” highlights Putonti. “This study is the first to broadly survey the lysogenic bacteriophage population within the urinary microbiome. We are now dedicating our efforts to more thoroughly investigate the possible associations between individual bacteriophages and/or bacteriophage prevalence and urinary health.”

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