



CAIRIBU UROBIOME RESEARCH INTEREST GROUP (U-RIG)

CAIRIBU U-RIG RESEARCH HOURS

EXECUTIVE SUMMARY 10/17/2025 U-RIG RESEARCH HOUR

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FEAT: NICOLE GILBERT, PHD,
MICHAEL NEUGENT, PHD

10/17/25 [3-4PM ET]

(2PM CT | 12PM PT)



Goal: Facilitate knowledge exchange and spur collaborations in the urobiome and adjacent fields

Summary

Dr. Nicole Gilbert: Strain-level heterogeneity in *Gardnerella* - covert pathogenesis in the bladder

Background on *Gardnerella* in the Urogenital Niche

- Dr. Gilbert provided background on *Gardnerella* in the urogenital tract, noting its common presence in urobiome data sets and its link to bacterial vaginosis (BV). *Gardnerella* is a frequent member of the urinary microbiome, often isolated in patients with a history of recurrent urinary tract infections or urgency urinary incontinence.
- Dr. Gilbert discussed the historical debate on *Gardnerella*'s role in pathogenesis, highlighting its initial identification in 1955 and subsequent debates over its pathogenic role in BV.

Genetic Diversity and Taxonomy of *Gardnerella*

- Dr. Gilbert explained the complex taxonomy and genetic diversity of *Gardnerella*, noting that it has been divided into four clades and various ecotypes over the years, though investigators still debate whether all strains are pathogenic, and if so, which ones. This debate stems from BV not always being symptomatic and inconsistent associations with lower urinary tract symptoms between studies.
- **Her research focuses on *Gardnerella*'s potential to exacerbate urinary tract infections (UTIs) caused by uropathogenic *E. coli*.**
 - Studies in mouse models showed that *Gardnerella* can worsen *E. coli* UTIs by increasing acute bacteria, persistent infection, and bladder titers in bacterial reservoirs and can trigger *E. coli* to come out of reservoirs to cause a recurrent infection.
 - Dr. Gilbert's studies were conducted with a clade 2 strain.

Mouse Model Studies and Covert Pathogenesis

- Dr. Gilbert hypothesized that the pathogenesis of *Gardnerella* in the urogenital niche was going to be clade or strain specific.
- Work by Lokesh Kumar, PhD in Dr. Gilbert's lab compared different *Gardnerella* strains from across four major clades in a mouse model of urinary tract infections.
 - Two clade 2 *Gardnerella* strains persisted longer in the urinary tract, causing urothelial disruption and covert pathogenesis.
 - Bladder staining revealed varying degrees of bladder exfoliation across *Gardnerella* strains.
 - Clade 2 and Clade 4 strains induced epithelial exfoliation and edema in the bladder. One of the clade 3 strands also induced edema.
 - **The ability of *Gardnerella* strains to cause pathogenic effects in the bladder was not related to isolation** (whether they originated from a vaginal swab or urine).
 - Persistence was not required to induce exfoliation or edema.
 - Exfoliation was not required for clearance. Exfoliation and edema appeared to be independent.

Genomic Analysis and Potential Biomarkers

- Collaboration with Dr. Robert Potter led to the analysis of whole genomes of 18 *Gardnerella* isolates, identifying 45 genes associated with various phenotypes.
- The genes identified include those related to colonization, exposure, exfoliation, and edema, with some genes suggesting surface exposure and interaction with the host.
- A pan-genome analysis of 291 publicly available *Gardnerella* genomes showed that persistence and exposure genes were conserved in Clade 2 and exfoliation genes were conserved in Clade 4 strains. Most genes were absent in Clade 3.

Summary and Implications

- Most *Gardnerella* do not persist in the urinary tract.
- Clade 2 and Clade 4 appear to be more pathogenic, at least to urothelium and bladder tissue. Clade 1 strains appeared to be benign.
- Dr. Gilbert noted that her studies were conducted in naïve young mice with healthy bladders. *Gardnerella* strains not pathogenic in a healthy naïve bladder could be revealed to be pathogenic in a more vulnerable context such as in an aged bladder or during pregnancy.

Dr. Gilbert is an Assistant Professor of Pediatrics, Infectious Diseases, Molecular Microbiology, and Obstetrics & Gynecology at Washington University. She is also active in the CAIRIBU Urobiome Research Interest Group.

Dr. Michael Neugent: Biochemical ecology of postmenopausal urobiome

Introduction

- Dr. Neugent emphasized the global health burden of recurrent UTIs in postmenopausal women, and how current treatment options (antibiotics) are unsustainable. Therefore, he stated, ***recurrent UTI treatment requires personalized approaches to management that consider the unique characteristics of each UTI and the impact of host factors.***

Study of Postmenopausal Urobiome and Microbial Ecology

- A human cohort study with clinical collaborator Dr. Philippe Zimmern at UT Southwestern included women with a history of recurrent UTI and healthy comparators.
- The study used whole genome metagenomic sequencing to capture the microbial and functional profiles of the urine samples.
- The cohort was highly phenotyped, with extensive clinical metadata and a fungal and bacterial isolate biobank for further testing.
- The study found that ***women with a history of recurrent UTI have increased dysbiosis and anti-microbial resistance genes***, even in the absence of infection. Those with no UTI history had increased lactobacillus – believed to be protective – and a lack of antimicrobial resistance genes.

Integration of Microbial Ecology and Biochemical Ecology

- Dr. Neugent's current work integrates microbial ecology and biochemical ecology to understand the context of the postmenopausal urobiome.
- Returning to the cohort study from before, metabolomic screening measure 630 different metabolites in the urine samples.
 - A significant but weak association between microbial diversity and biochemical diversity was found, with high abundant taxa associated with low abundant metabolites.
 - Two metabolites, methionine sulfoxide and trimethylamine oxide, were strongly correlated with microbial alpha diversity, suggesting a link to local oxidative stress.
- The study identified a lipid signature that distinguishes infected from non-infected samples, with a 12-lipid model showing high accuracy in identifying active infections. The lipid signature correlates strongly with known uropathogens, particularly *Escherichia coli*.

Diagnostic and Prognostic Biomarkers in Urobiome

- A Cox hazard model identified 12 metabolites associated with time to recurrence, with deoxycholic acid being the most strongly associated.
- The study suggests that deoxycholic acid could be a prognostic biomarker for recurrent UTIs, with further validation needed.

Dr. Neugent is a postdoctoral research associate at the University of Texas at Dallas in Dr. Nicole De Nisco's laboratory. Dr. Neugent is one of the leaders of the CAIRIBU Urobiome Research Interest Group.
