



CAIRIBU UROBIOME RESEARCH INTEREST GROUP (U-RIG)

CAIRIBU U-RIG RESEARCH HOURS

EXECUTIVE SUMMARY 1/24/2025 U-RIG RESEARCH HOUR

U-RIG RESEARCH HOUR

FEAT: KATY PATRAS, PHD, SETH REASONER,
MD/PHD CANDIDATE

THE VAGINAL MICROBIOTA AND COLONIZATION BY UROPATHOGENS
PATHOGEN EVOLUTION IN NEUROGENIC BLADDER

1/24/25 [3-4PM ET]



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

Summary

Dr. Katy Patras' Presentation

Background

- The Patras Lab focuses on women of reproductive age, who are more susceptible to urinary tract infections (UTIs). The Patras Lab aims to understand the origin of urinary pathogens and their colonization sources.
- Dr. Patras mentioned various existing theories for why women are more susceptible to UTIs, including anatomical differences, hygiene, and hormones.

Sources of Urinary Pathogens

- Dr. Patras cited that *E. coli* is the most common pathogen associated with uncomplicated UTIs.
- She discussed the role of the gut and urinary reservoirs in harboring these pathogens.
- **The vaginal microbiota is a potential additional reservoir for urinary pathogens.**
- Dr. Patras highlighted a study from Dr. Wolfe's group showed similarities between the bladder and vaginal microbiomes, suggesting shared organisms.

Vaginal Microbiota and Its Role in UTIs

- Dr. Patras described the vaginal microbiota as unique and has low alpha diversity and dominance by lactobacilli.
- Potential urinary pathogens like streptococcus, staphylococcus, and Enterococcus are present but in lower abundance. Moreover, the community state-type composition of the vaginal microbiome is linked to increased risk for urogenital infections.
- **Studies show higher vaginal *E. coli* colonization in women with recurrent UTIs compared to controls.**

Inhibitory Effects of Lactobacillus on *E. coli*

- Dr. Patras said that Lactobacillus dominance in the vaginal microbiota is associated with lower *E. coli* colonization.
- In vitro studies show anti-*E. coli* activity in vaginal lactobacilli, with some strains significantly inhibiting *E. coli* growth.
- **A study with Lactin V, a bio-therapeutic candidate, demonstrated protective effects against recurrent UTIs in women with higher levels of lactobacilli.**
- Dr. Patras emphasized the need for better preclinical models to predict effective bio-therapeutics.

Developing Preclinical Models for Vaginal Microbiota

- **The Patras Lab has developed mini bioreactors to model the vaginal microbiota in vitro.**
- The bioreactors mimic the nutrient and fluid turnover of the vaginal tract.
- Human vaginal organoids are used to model the vaginal epithelium and test therapeutics.
- The organoids demonstrate high levels of keratin and other proteins expected in the vaginal epithelium.

Synthetic Communities and Phage Therapy

- The Patras Lab is developing synthetic communities of vaginal isolates to inhibit pathogens and modulate the host response.
 - Three synthetic communities have been tested for their ability to inhibit *E. coli* and modulate host response.
 - Bacteriophage are also being studied for their potential to reduce vaginal colonization of *E. coli*.
 - A mouse model of vaginal *E. coli* colonization is being used to test the efficacy of phage therapy.

Challenges and Future Directions

- The mouse model shows modest effects of phage therapy, with statistical significance but low impact.
- The Patras Lab plans to explore the role of phage cocktails and the host reservoir for pathogenic bacteria.
- Future directions include pairing microbial samples with organoid lines to study host-specific interactions.

Katy Patras, PhD is an Assistant Professor of Molecular Virology and Microbiology at Baylor College of Medicine. She completed her post-doctoral fellowship at UC San Diego. The Patras Lab focuses on the vaginal microbiota and its role in urogenital health and disease. They are keenly interested in host-microbe interactions as they pertain to overall urogenital health and bacterial pathogenesis, with focus on urinary tract infections, vaginal colonization, pregnancy and diabetes.

Seth Reasoner's Presentation

Background

- Seth introduced the project he is working on which is to understand **bacterial evolution in the urinary tract of patients with neurogenic bladder.**
- His research focuses on patients with spina bifida, who have high rates of UTIs due to chronic colonization and frequent catheterization.
- The cohort he and his collaborators have assembled includes nearly 100 patients from two medical centers, with prospective and retrospective sample collection.
- **Whole genome sequencing of bacterial isolates has revealed cross-species evolution in iron acquisition and O antigen biosynthesis genes.**

Longitudinal Analysis of Bacterial Isolates

- Seth cited variability in species and strains within individual patients, with frequent recolonization after antibiotic treatment.
- Cross-species mutations in iron acquisition genes and O antigen biosynthesis genes have been identified.
- The *y w* gene, involved in O antigen biosynthesis, has shown a premature stop codon in clinical isolates.
- **In vitro experiments confirm that *y w* mutations lead to truncated LPS and reduced swimming motility.**

Implications and Future Research

- Seth shared that the *y w* mutation reduces phagocytosis by macrophages and promotes survival within macrophages.
- **Overall, results suggest that loss of O antigen may modulate immunogenicity and contribute to bacterial persistence.**
- Future research includes testing the effect of O antigen loss in a mouse model of urinary tract infection.
- The group will continue to collect samples to understand long-term dynamics of the urinary microbiome and bacterial evolution.

Seth Reasoner is an MD-PhD student in the Microbe-Host Interactions program at Vanderbilt University in the lab of Maria Hadjifrangiskou, PhD. Seth Reasoner's research interests include the connection of bacteria to human health and disease. Specifically, he studies bacterial signaling and metabolism.