



CAIRIBU UROBIOME RESEARCH INTEREST GROUP (U-RIG)

CAIRIBU U-RIG RESEARCH HOURS

EXECUTIVE SUMMARY 2/21/2025 U-RIG RESEARCH HOUR

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FEAT: KYMORA SCOTLAND, MD, PHD, JASHKARAN GADHVI, PHD

BIOFILM- FORMING BACTERIA DRIVE CALCIUM OXALATE KIDNEY STONE PROPAGATION

UNDERSTANDING THE ROLE OF HOST ADAPTIVE IMMUNE RESPONSE TO RECURRENT URINARY TRACT INFECTION

2/21/25 [3-4PM ET]



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

Summary

Dr. Kymora Scotland's Presentation

Dr. Kymora Scotland's Research on Kidney Stones and Bacteria

- Dr. Kymora Scotland's research focus is on the role of bacteria in kidney stone formation.
- She described the multifactorial nature of kidney stone formation, mentioning diet, immunity, heavy metals, genetics, hormones, and bacteria as potential contributing factors.
- Traditional thinking has linked bacteria to urinary tract stones, but Dr. Scotland noted that calcium oxalate stones, the most common type, are generally considered non-infectious.
- She shared her observations of infected calcium oxalate stones and the presence of bacteria in stone cultures, even in patients without a history of urinary tract infections.

Methods for Exploring the Role of Bacteria in Kidney Stone Formation

- Dr. Scotland described the layering patterns in calcium oxalate stones, similar to stromatolites formed by microbial activity.
 - She uses three-dimensional X-ray tomography to analyze the layering in kidney stones.
 - Using scanning electron microscopy, Dr. Scotland identifies bacteria within the internal structure of calcium oxalate stones.
 - She conducts *in vitro* experiments to study the impact of bacteria on calcium oxalate crystals, showing that bacteria can alter crystal morphology and increase crystal aggregation.
 - Her team has developed a microfluidic system to study the effects of bacterial secretions on crystal growth and formation kinetics.

Research Findings

- Potential mechanisms by which bacteria influence crystal formation **include changes in pH, bacterial secretions, and adhesion to crystals.**
- Bacteria appear to alter the pH to promote crystal aggregation within optimal pH ranges, similar to urine.
- **Bacterial secretions, including extracellular DNA (eDNA), play a significant role in calcium oxalate crystal formation and aggregation.**

Conclusions and Future Directions

- Dr. Scotland concludes that **biofilm-forming bacteria alter calcium oxalate crystal morphology and increase crystal aggregation**.
- She collaborates with Henry Schreiber's team to extract bacteria from kidney stones and study their role in stone formation.
- Dr. Scotland's team plans to develop a system to study the effect of bacteria on actual kidney stones using a 3D kidney model.

Kymora Scotland, MD, PhD is an Assistant Professor of Urology and Director of Endourology Research and Associate Director of the Endourology Fellowship Program at UCLA. Dr. Scotland's clinical expertise is in kidney stone treatment and benign prostatic hyperplasia management. Her research aims to determine the role of bacteria in the growth of calcium-based kidney stones and the significance of bacteria to kidney stone disease.

Jashkaran Gadhvi's Presentation

Dr. Jashkaran Gadhvi's Research on Adaptive Immune Response to Recurrent UTI

- Dr. Gadhvi's PhD research focuses on the host adaptive immune response to recurrent urinary tract infections (UTI).
- He explained the cycle of UTI infection, including the role of bacteria and the host immune response.
- He described the **innate immune response to UTI**, which includes cytokine and chemokine release, neutrophil infiltration, and monocyte differentiation.
- He described the **adaptive immune response**, focusing on the role of T cells and B cells in generating immune memory.

Study of Adaptive Immune Response in Human Recurrent UTI

- Dr. Gadhvi's team collects biopsy tissue samples from postmenopausal women with recurrent UTI.
- They find lymphoid follicles filled with T cells and B cells in inflamed regions, suggesting an active adaptive immune response.
- Immunofluorescence confocal microscopy reveals enrichment of CD4+ T cells in inflamed regions.
- **Dr. Gadhvi's team hypothesizes a T helper 2 (Th2) bias in the bladder, which may diminish the ability to provide long-term immunity.**

Analysis of Cytokine Levels and Humoral Immune Response

- Urinary cytokine levels in different patient cohorts are measured.
- They have **identified elevated levels of IL-2, IL-22, IL-6, and IL-10**.
- They have also detected **elevated levels of IgG in the urine of patients with active UTI**, with specific isotypes being highly abundant.
- Dr. Gadhvi's team proposes future studies to characterize regulatory immune cell populations and investigate the role of cytokines as diagnostic markers.
- They plan to understand the specific targets and roles of antibodies in recurrent UTI.

Conclusions and Future Research Directions

- Dr. Gadhvi concluded that lymphoid follicles and elevated cytokine levels suggest an active adaptive immune response in recurrent UTI.
- Future studies will characterize regulatory immune cell populations and investigate the role of cytokines as diagnostic markers.
- A primary goal is to understand the specific targets and roles of antibodies in recurrent UTI.

Jashkaran Gadhvi, PhD is a postdoctoral fellow in Doug Strand's lab at UT Southwestern. Dr. Gadhvi completed a PhD in the lab of Nicole De Nisco, PhD in Cellular and Molecular Biology at the University of Texas at Dallas. During his doctoral studies, Jash studied the host adaptive immune response during recurrent urinary tract infections in post-menopausal women.