



CAIRIBU UROBIOME RESEARCH INTEREST GROUP (U-RIG)

CAIRIBU U-RIG KNOWLEDGE EXCHANGES

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

EXECUTIVE SUMMARY 04/17/2026 U-RIG KNOWLEDGE EXCHANGE



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FEAT: XINTONG DONG, PHD,
KYMORA SCOTLAND, MD, PHD

Summary

Dr. Xintong Dong's Presentation: Antimicrobial peptide signaling in urinary tract infections

Introduction

- Dr. Dong's lab studies the functions of antimicrobial peptides (AMPs) across a number of epithelial barriers – including skin, airways, intestines, and urogenital tract
- Few AMPs are expressed in a healthy state – the ones that are there are not very charged and keep the microbiota in balance
- Infection, inflammatory diseases, or other immune dysregulation leads to inflamed epithelial cells and increased production of AMPs

AMP and MRGP functionality

- Dr. Dong's lab and other labs found AMPs perform signaling functions. Innate immune cells express a cell type-specific G-protein-coupled receptor (GPCR) allowing them to respond to AMP signals.
- These GPCRs belong to a larger family called mast-related G-protein couple receptors, also known as MrGs
- Major AMP families in mammalian systems are defensins and cathelicidin
- Ligand receptor interactions between AMPs and GPCRs are based on charge
- The more charges that defensins or cathelicidin bear, the more likely receptors are to be activated
- In mice, tissue-resident cells performing a sentinel function (sensory neurons, mast cells) are more sensitive and respond to peptides at lower EC50
- In contrast, infiltrating inflammatory cells (neutrophils) are less sensitive, responding only to the most cationic peptides.
- Single and double cluster knockouts, cre lines, and humanized mouse lines allowed Dr. Dong and her mentor to explore the loss of functions in each receptor in their corresponding cell types and contexts.

AMP signaling in xkin

- Deleting defensin peptides in mice resulted in *S. aureus* spreading to a much larger area and higher bacterial burdens through the course of infection, causing a much larger necrotic lesion
- Knocking out just the neutrophil receptor - Mrgpra2 - resulted in a nearly identical phenotype, demonstrating the importance of peptide signaling functions
- In a skin *S. aureus* infection, neutrophil abscess formed around the site of infection. In the absence of defensins or the neutrophil receptor, the abscess is largely defective, and bacteria spread to a larger area. The mechanism behind this is that ablation of defensins or Mrgpra2 receptor jeopardizes the neutrophil pro-inflammatory signaling loop that recruits more neutrophils.

AMP signaling in the bladder and UTI

- Bladder epithelial cells express a number of defensins, some overlapping with those of the skin, and an analogous immune system
- Skin interfaces with air, while the bladder interfaces with liquid. **The two organs have vastly different microbiota and tissue-specific phenotypes.**
- Now in Aim 1 of her Katz R01, Dr. Dong is developing a **bladder-specific defensin knockout**. In Aim 2, she will study the immune modulatory functions of defensins. In Aim 3, she will look at how sensory neurons contribute to UTI pain and neuroimmune interaction.

Mast cell receptor Mrgprab2 in UTI

- b2 recruits neutrophils during infection
- In b2 knockout mice, phenotype observed was reduced immune cell infiltration and increased urine bacterial burden
- Mast cell-urothelial cross-talk impacts b2 urothelial gene expression and exfoliation (ongoing research to understand molecular mechanisms and therapeutic targets with the goal of treating UTI by reducing bacterial load, inflammation and pain)

Dr. Kymora Scotland's Presentation: Kidney Stones Harbor Bacterial Bunkers

Introduction

- Kidney stone disease (KSD) is a painful condition affecting over 10% of Americans, though much is unknown about urolithiasis pathogenesis. Pathogenesis is multifactorial – with genetic, dietary, and immunity contributors.
- Specific bacteria are known to cause struvite stones, which make up a small population of stones
- **But roughly 80% of stones are calcium oxalate (CaOx) stones, which are not thought to be associated with bacteria**
- Dr. Scotland was interested in investigating if kidney stones and UTIs are connected given that kidney stone formers are at significantly increased risk of UTI

Bacterial biofilms in kidney stones

- Previous research identified bacteria during sequencing of CaOx, such as *E. coli* or pseudomonas. These bacteria are distinct from those found with struvite stones.
- In collaborative work with Henry Schreiber, PhD, she showed bacteria were able to be extracted from kidney stones from patients with no history of UTI
- *E. coli* adheres to calcium-based crystals and form stone-like encrustations on kidney stents
- **Hypothesis: uropathogenic bacteria promote CaOx stone growth using the same biofilm tools**

Biominingalization

- Biominingalization is the deposition of minerals in specific patterns and is often influenced by microorganisms
- To better understand kidney stone mineral and organic substructures, her team conducted XRM/XRF fusion imaging
 - Stratigraphic evaluations of stone layers revealed biogenic components. Just as in the layering or stromalites, microbial mat activity (similar to biofilm deposition) was found in kidney stones
 - CaOx stones were observed to have layering of minerals and organics and large voids
- Staining revealed bacteria as well as biofilm material even in the absence of infection
- Bacteria within stones is often polymicrobial, with several species being those expected in UTIs; this supports the hypothesis that uropathogens play a role in kidney stone growth
- The presence of biofilm alters crystallite nucleation in stone layers. In organic areas of stones, more nucleation was linked to smaller mineral domains. Farther from the organic layers, crystal size was larger.

Dissolution of stones and bacteria

- Voids in CaOx stones are areas of dissolution. CaOx stones can be monohydrate or dihydrate and CaOx dihydrate stones can dissolve and reform. **Dr. Scotland hypothesized that dissolution provides opportunity for bacteria to survive.**

Ongoing and future work

- She found that bacteria localize to crystals and cause an increase in the formation kinetics, increasing the size, number and aggregation of crystals *in vitro*
- She has associated etchings in crystals associated with organic material, which may be helping them twin and aggregate
- Dr. Scotland is working on developing real time Raman spectroscopy to correlate with micro-CT to continue to examine bacteria within stones. Biofilm exists even within mineral layers. Biofilm structures are thought to trigger increased growth rates of mineral layers. Moving forward, she wants to explore if biofilm is necessary for this phenomenon
- Additionally, she is developing a microfluidic kidney model to study biofilm formation and its impact on stone growth

Xintong Dong, PhD is Assistant Professor of Biological Sciences at the University of Texas at Dallas. Her lab uses mouse genetic models to study antimicrobial peptide functions in host-microbe crosstalk and neuroimmunity.

Kymora Scotland, MD, PhD, is Assistant Professor and Chief of Endourology Research at UCLA. Her clinical interests include the treatment of kidney stones, benign prostatic hyperplasia and upper tract urothelial carcinoma. Her basic research investigates stone pathogenesis, stone-associated infection and the physiology of peristalsis. She has a particular clinical research interest in developing techniques aimed at improving quality of life for nephrolithiasis patients and has focused recent work on patient engagement with medical management regimens.