



CAIRIBU UROBIOME RESEARCH INTEREST GROUP (U-RIG)

CAIRIBU U-RIG RESEARCH HOURS

EXECUTIVE SUMMARY 3/21/2025 U-RIG RESEARCH HOUR

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**FEAT: EMILY COFFEY, DVM, DACVIM, PHD,
ADWAITA PARAB, MS, PHD CANDIDATE**

**LESSONS LEARNED FROM CANINE UROBIOME RESEARCH
BLADDER EPITHELIUM-DERIVED ORGANIDS: A NEW MODEL TO
INVESTIGATE THE ROLE OF METABOLISM IN AGING**

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



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

Summary

Dr. Emily Coffey's Presentation: Synergy between veterinary science and urobiome research

Introduction and Overview of Dr. Emily Coffey's Presentation

- Dr. Coffey introduced the dog as a potential model for understanding the urobiome.
- She emphasized that her presentation will be "data-light," focusing more on sparking collaboration and brainstorming ideas.

Advantages of Using Dogs as a Model for Urobiome Research

- She reviewed advantages of using dogs as a model for studying the urobiome, including their similarity to humans in terms of urogenital disorders.
- She highlighted the larger bladder capacities and longer life spans of dogs compared to traditional animal models like laboratory rodents.
- She noted similarities in immune system development and function between dogs and humans as well as similar shifts in gut microbiome composition in response to dietary stimuli.
- She noted the genetic diversity within dog breeds, which can be beneficial for case-control studies, and the shared environmental exposures between dogs and humans.

Challenges and Disadvantages of Using Dogs as a Model

- Dr. Coffey acknowledged disadvantages of using dogs as a model, including their different genetics and physiology compared to humans.
- She discussed ethical implications of using animal models and challenges of working with spayed and neutered dogs, which constitute the majority of dogs in the United States.
- She noted behavioral differences in dogs, such as grooming behaviors, which can influence the urobiome.
- She highlighted logistical challenges of working with client-owned animals, including compliance with diet and clinical signs monitoring.

Specific Disease Microbe Associations and Patient-Specific Variables

- Dr. Coffey focused on specific disease microbe associations, particularly urolithiasis, and similarities between dogs and humans in terms of bladder neoplasia and neurogenic bladders.
- **Prior findings have shown lower microbial diversity in the gut microbiome of dogs with renal stones and deficiencies in SCFA-producing bacteria**, both of which are similar to humans with stones.
 - Differences in urine microbiome composition between stone formers and healthy controls include enrichment of certain bacteria like *Pseudomonas* and *Fusobacteria*.
- Data also demonstrate, she said, the impact of diet on urobiome composition. Specifically, differences between dogs on diverse diets vs. those on singular diets are known.

Experimental and Technical Needs in Urobiome Research

- Dr. Coffey discussed experimental and technical needs in urobiome research, which include collection of urine samples using different techniques like natural voiding and cystocentesis. Data demonstrate differences in bacterial composition.
- She highlighted challenges of working with large volume, low biomass liquid samples and potential benefits of using small vacuum filtration methods.
- **She emphasized importance of cross-disciplinary research and public engagement in urobiome research**, noting potential for collaboration between different fields and the public's interest in animal health.

Bridging the Clinical Divide and Future Directions

- Dr. Coffey discussed potential to bridge the clinical divide by using dogs as models for interventions that are not yet ready for human testing.
- She mentioned planned studies on dietary strategies, bionotics, and impact of FMT on urobiome composition.
- She highlighted opportunities for leveraging the dog model to study conditions like recurrent UTI and neurogenic bladders.
- She concluded by expressing willingness to collaborate with others within the group.

Emily Coffey, DVM, DACVIM, PhD, is an Assistant Professor of Small Animal Internal Medicine. Her research focuses on understanding the role of the microbiome in health and disease. She has a particular interest in the urobiome and the effects of host microbial communities and biological metabolites on urinary stone formation. She hopes to apply discoveries about the microbiome to improve healthcare for both humans and animals.

Adwaita Parab's Presentation: A bladder epithelium-derived organoid model to study aging

Introduction and Overview of Adwaita's Research on a Bladder Epithelium-Derived Organoid Model

- Adwaita explained advantages of organoids, including their ability to provide an organotypic structure, reduced costs for research, and ability to study relevant pathways.
- She described the process of developing mouse bladder organoids, including the acquisition of bladders, cell lysis, and differentiation into epithelial cells.
- She characterized the organoids using H&E staining and immunofluorescence for urothelial markers to confirm the presence of epithelial cell markers.

Characterization of Aged Bladder Organoids

- Adwaita discussed cellular changes observed in aged organoids, including dysregulated differentiation, increased inflammation, and increased UTI risk.
- Findings thus far include:
 - **Slower differentiation rates in aged organoids**
 - **Higher levels of lysosomes and more active mitochondria in aged organoids**
 - **Lower antioxidant response and higher levels of ROS**

Infection and Co-Culture Studies with Aged Organoids

- Adwaita described how she co-cultures young and aged organoids with macrophages to reconstruct the immune system and assess the interaction between epithelial cells and immune cells.
- She described how she infects young and aged organoids with GFP-tagged uropathogenic *E. coli* (UPEC) and quantifies the intracellular bacteria using fluorescence.
 - Aged vs. young organoids have more UPEC present inside them at 3 hours post-infection
- She explained how she generates genetic knockout organoids, specifically IRG1 knockouts, to study metabolic pathways associated with aging.

Metabolomics and Supplementation Studies

- Adwaita explained that she performs unbiased metabolomics on young and aged organoids and has identified **41 metabolites that are differentially altered between the two groups**.
- She then reviewed how she maps these metabolites to metabolic pathways and has found **significant changes in purine metabolism, glycerol phospholipid metabolism, and glycine, serine, threonine metabolism**. She has also demonstrated that supplementation of aged organoids with D-mannose and nicotinamide results in reduced oxidative stress and DNA damage markers.
- Adwaita concluded by highlighting the potential of organoid model to address current challenges in aging studies and to develop personalized therapies for UTIs.

Adwaita Parab is a graduate student in the lab of Indira Mysorekar, PhD at Baylor College of Medicine. Adwaita is currently pursuing her PhD in Immunology and Microbiology. Her research goal is to find key molecular mechanisms underlying diseases and hence develop targeted therapies. Under the mentorship of Dr. Mysorekar, Adwaita studies metabolic alterations that drive aging in the female urinary bladder and increase susceptibility to urinary tract infections in postmenopausal women.