



CAIRIBU UROBIOME RESEARCH INTEREST GROUP (U-RIG)

CAIRIBU U-RIG RESEARCH HOURS

EXECUTIVE SUMMARY 12/15/2023 U-RIG RESEARCH HOUR

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



FRIDAY, DEC 15
3:00 PM ET
2 PM CENTRAL | 12 PM PACIFIC

SPEAKERS



Lisa Karstens, PhD

Assistant Professor
Oregon Health and Science University
Department of Medical Informatics and Clinical Epidemiology
Department of Obstetrics and Gynecology



Jeremy P. Burton, PhD, MSc

Chair in Human Microbiome and Probiotics
Associate Professor, Division of Urology, Departments of Surgery/ Microbiology & Immunology,
Western University
Scientist, Lawson Health Research Institute, St. Joseph's Hospital
Canadian Centre for Human Microbiome and Probiotics

NOTES FROM PRESENTATIONS BY DR. BURTON AND DR. KARSTENS

The relationship between microbiome and urogenital health

- Dr. Jeremy Burton discussed the relationship between commensal bacteria and human health
- He noted the interconnectedness of the microbiome, including its influence on urology and the potential for microorganisms to cross over to other sites such as the gastrointestinal and periodontal tracts
- New technologies and models are being developed to better understand urological conditions, including the use of *Drosophila* (in kidney stone research), spheroid models, and imaging techniques to directly visualize

Using MRI to visualize microbes in the body

- The potential of MRI and PET-MRI for microbiome research was reviewed and includes potential applications for tracking persistence and colonization
- MRI may be useful in studying the return of microbes in the genital tract, including in bladder cells
- He has identified that different microbes have different returns under different metal uptake conditions; returns are influenced by the metals they take up
- Genetic targets for radioactive probes were presented, citing experiments in which one of these genes was transferred into an *E. coli* strain of interest to see if it returned an MRI signal

Labeling microbes with radioactive isotopes for imaging

- Genes from magnetotactic bacteria may add contrast to MRI images of bacteria, potentially allowing for better visualization of specific microorganisms

- New methods to label microbes with radioactive tracers for imaging and tracking in the body were reviewed, including using probiotics labeled with radioisotopes to track movement through digestive system *in vivo*

Optimizing information for investigating the urobiome

- Dr. Lisa Karstens is an assistant professor at Oregon Health and Science University who studies the human microbiome in health and disease, particularly in women's health and bladder disorders
- She reviewed how Dr. Wolfe's work founded the concept of a resident microbiome in the bladder; Dr. Karstens is building upon this research in her interdisciplinary group at OHSU
- Various methods to analyze urine samples are used, including shotgun metagenomics and marker gene sequencing, to identify and study microbial communities without isolating or growing them

Female and male urinary microbiomes and their characteristics

- Studies show that the typical female urinary microbiome is a poly microbial community dominated by *Lactobacillus*, *Gardnerella*, and other bacteria; the male urinary microbiome is more diverse and has not been directly compared to the female microbiome
- Dr. Karstens highlighted the challenges of studying the urobiome, including low microbial biomass and limited knowledge compared to other body sites
- Challenges in sequence-based studies were discussed, e.g., contaminant DNA detection

Contamination in sequencing studies and methods to address it

- She discussed the importance of controlling for contaminants in microbiome sequencing studies, highlighting the need for mock communities and serial dilutions to account for potential sources of bias
- A benchmarking study to evaluate the effectiveness of different computational methods for removing contaminants from sequencing data showed promising results
- She explained how the negative control filter in their sequencing data performed poorly, highlighting the need for careful experimental design and parameterization
- The importance of using multiple methods and considering additional information was stressed, such as DNA concentration, to accurately detect contaminants in sequencing studies

Bacterial taxonomy and glycans in urinary tract infections

- The importance of using a comprehensive reference database for bacterial taxonomy assignment was reviewed; NCBI 16s database is most effective
- Dr. Karstens reviewed studies exploring beyond bacterial taxonomy, focusing on the relevance of sequencing data and potential for bioinformatics problems when filtering by *Lactobacillus*
- Urine from women with overactive bladder revealed differences in glycan structures; specifically, specific glycosaccharides were altered in urine of women with urinary urgency and frequency but not incontinence

Decontaminating metagenomic data

- Robust methodologies, sharing data, and adherence to community standards were emphasized
- Decontamination strategies for shotgun metagenomic data were reviewed

NOTES FROM Q&A

Using pigs for imaging and disease modeling

- The group discussed limitations of using MRI to track bacterial translocation in animal models
- Question was asked about using a full pig model for imaging purposes

Gut microbiome research and imaging techniques

- Use of functional imaging modalities to study the gut microbiome (MRI and PET scans) was discussed
- Potential for real-time imaging to observe reactions and behavior to interventions was discussed
- Targeted functional prediction tools vs the use of broad tools for specific questions was suggested
- The group iterated importance of sequencing data to correlate bacterial information with glycan levels

Microbiome analysis and its applications in healthcare

- Clinical implications of modifying glycans in the bladder wall to influence microbial growth was discussed
- Differences in glycan genes among bacteria were noted; presence alone does not determine functionality
- The group discussed megatrends in metabolomic urine analyses, minding limitations of taxonomy-based analysis, including dormant bacteria

Recent publications Dr. Jermei Burton:

1. Routy, B., Lenehan, J. G., Miller Jr, W. H., Jamal, R., Messaoudene, M., Daisley, B. A., ... & Maleki Vareki, S. (2023). Fecal microbiota transplantation plus anti-PD-1 immunotherapy in advanced melanoma: a phase I trial. *Nature medicine*, 29(8), 2121-2132.
2. Al, K.F., Joris, B. R., Daisley, B. A., Chmiel, J. A., Bjazevic, J., Reid, G., ... & Burton, J. P. (2023). Multi-site microbiota alteration is a hallmark of kidney stone formation. *Microbiome*, 11(1), 263.
3. Daisley, B. A., Pitek, A. P., Torres, C., Lowery, R., Adair, B. A., Al, K. F., ... & Niño, E. (2023). Delivery mechanism can enhance probiotic activity against honey bee pathogens. *The ISME Journal*, 1-14.
4. Chmiel, J. A., Stuivenberg, G. A., Al, K. F., Akouris, P. P., Razvi, H., Burton, J. P., & Bjazevic, J. (2023). Vitamins as regulators of calcium-containing kidney stones—new perspectives on the role of the gut microbiome. *Nature Reviews Urology*, 1-23.
5. Ninkov, M., Schmerk, C. L., Moradizadeh, M., Parvathy, S. N., Figueredo, R., Burton, J. P., ... & Haeryfar, S. M. (2023). Improved MAIT cell functions following fecal microbiota transplantation for metastatic renal cell carcinoma. *Cancer Immunology, Immunotherapy*, 72(5), 1247-1260.
6. Stuivenberg, G. A., Chmiel, J. A., Akouris, P. P., White, J., Wilcox, H., Seney, S., ... & Reid, G. (2023). Supplementing Yogurt with Probiotic Bifidobacteria to Counter Chronic Kidney Disease. *Fermentation*, 9(4), 391.
7. Gholami, H., Chmiel, J. A., Burton, J. P., & Maleki Vareki, S. (2023). The Role of Microbiota-Derived Vitamins in Immune Homeostasis and Enhancing Cancer Immunotherapy. *Cancers*, 15(4), 1300.
8. Chmiel, J. A., Carr, C., Stuivenberg, G. A., Venema, R., Chanyi, R. M., Al, K. F., ... & Burton, J. P. (2023). Corrigendum: New perspectives on an old grouping: the genomic and phenotypic variability of Oxalobacter formigenes and the implications for calcium oxalate stone prevention. *Frontiers in Microbiology*, 14, 1231746.
9. Al, K. F., Allen, L., Bedell, S., Burton, J. P., & de Vrijer, B. (2023). Assessing the impact of pregnancy and birth factors on the maternal and infant microbiota. *Microbiome Research Reports*, 2(4).

Recent publications from Dr. Lisa Karstens:

1. Altinok Dindar, D., Chun, B., Palma, A., Cheney, J., Krieger, M., Kasschau, K., ... & Zhang, Z. (2023). Association between Gut Microbiota and Breast Cancer: Diet as a Potential Modulating Factor. *Nutrients*, 15(21), 4628.
2. Kelliher, J. M., Rudolph, M., Vangay, P., Abbas, A., Borton, M. A., Davenport, E. R., ... & Eloe-Fadrosh, E. A. (2023). Cohort-based learning for microbiome research community standards. *Nature Microbiology*, 1-3.
3. Bowie, K., Garzotto, M., Orwoll, E., & Karstens, L. (2023). BMI and BPH correlate with urinary microbiome diversity and lower urinary tract symptoms in men. *bioRxiv*, 2023-12.
4. Carnes, M. U., Siddiqui, N. Y., Karstens, L., Gantz, M. G., Dinwiddie, D. L., Sung, V. W., ... & Eunice Kennedy Shriver National Institute of Child Health. (2023). Urinary microbiome community types associated with urinary incontinence severity in women. *American Journal of Obstetrics and Gynecology*.
5. Nakamura, Y. K., Metea, C., Llorenç, V., Karstens, L., Balter, A., & Lin, P. (2023). A diet rich in fermentable fiber promotes robust changes in the intestinal microbiota, mitigates intestinal permeability, and attenuates autoimmune uveitis. *Scientific Reports*, 13(1), 10806.
6. Martin, T. M., Karstens, L., Gill, T., Ogle, K., Davin, S., Fale-Olsen, E., ... & Rosenbaum, J. T. (2023). Altered fecal microbiome in birdshot chorioretinopathy compared to HLA-A29 positive healthy subjects. *Investigative Ophthalmology & Visual Science*, 64(8), 3576-3576.
7. Chun, B., Goodyear, S., Rice-Stitt, T., Karstens, L., Dahl, E., Li, A., ... & Zahi, M. (2023). Abstract P1-04-02: Gut microbiome diversity correlates with tumor PD-L1 status in metastatic triple negative breast cancer (mTNBC): correlative analysis of gut microbiome and tumoral biomarkers. *Cancer Research*, 83(5_Supplement), P1-04.