CAIRIBU UROBIOME RESEARCH INTEREST GROUP (U-RIG)

CAIRIBU U-RIG RESEARCH HOURS

EXECUTIVE SUMMARY 11/17/2023 U-RIG RESEARCH HOUR

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

NOTES FROM PRESENTATIONS BY DR. WOLFE AND DR. HADJIFRANGISKOU

Improving diagnostic testing and antibiotic susceptibility testing in UTI

- Dr. Wolfe discussed recent papers on urinary tract infection (UTI) diagnostic testing, highlighting limitations of standard urine culture and the need for improved tests to preserve antibiotic stewardship
- Reviewed insights on emerging uropathogens and importance of developing new diagnostic tests to improve treatment outcomes
- He noted role of lesser-known urinary tract pathogens, e.g., *Enterococcus faecalis* and *Actinomyceteaceae*

NYCIII as a growth medium for antibiotic susceptibility testing

- NYCIII replaces lysed horse blood with horse serum; supports growth of species not seen in MHB medium
- Dr. Wolfe endorsed NYCIII as growth medium for antibiotic susceptibility testing; results for fastidious and anaerobic microbes were comparable to MHB

Microbiota disruption and recovery after gynecological surgery

- The resilience of urogenital microbiota during and after gynecological surgery in pre- and post-menopausal females was reviewed; findings included disruption in bladder microbiome alpha diversity recoveries by 12 weeks post-surgery
- Pre-menopausal women's microbiota returned to baseline after surgery, **while post-menopausal women's microbiota remained altered**

Microbiome analysis in pre- and post-menopausal mice

- Dr. Wolfe presented data from urine samples collected from two sets of mice housed in different facilities; analysis for both groups used the same sequencing pipeline
- Mouse microbiome, specifically focusing on the predominant taxa, have proven sensitive to environmental conditions; similarities in the microbime of mice in different environments, using multiple sequencing and culture approaches, were found

Composition and dynamics of the urinary microbiome across the lifespan

- Dr. Hadjifrangiskou introduced her lab's focus on understanding how *E. coli* interacts with the host environment and with bacteria in biofilms
- She discussed interactions with uropathogens, highlighting need for more research on lifespan variations in the urobiome including in the healthy urobiome across different ages and sexes and also in people with conditions such as spina bifida

Infant urinary tract microbiome

- Results from studies in the microbiome of healthy infant males during circumcision (samples for which were collected from the operating room), have identified new species of bacteria in the infant male gut microbiome
- Further investigations in the role of actinotignum (actinobaculum) in shaping bladder pathogen interactions and UTI progression are ongoing

Growing rare bacteria in lab conditions

- Discussed the prevalence of Actinotignum in the population, with a focus on collecting urine samples from healthy individuals to determine how common these bacteria are
- Studies aim to identify the prevalence of Actinotignum across the population and to grow and genetically manipulate the bacteria to better understand their role in UTIs
- **Dr. Hadjifrangiskou invites collaborations with individuals who have connections with their clinical microbiology labs in order to extend this study geographically**
- She further addressed the use of lipids in bacterial growth, highlighting the success of incorporating 1% lipids into lab growth media for non-fastidious bacteria, and showed that myristic acid and arachidonic acid were sufficient to promote the growth of Actinotignum *in vitro*. Dr. Hadjifrangiskou asked, **could increases in arachindonic acid coincide with a bloom in Actinotignum in older men?**
- The first-ever scanning electron microscopy images of Actinotignum were shared (from the work of Hadjifrangiskou lab student Jamisha Francis) and showed the bacteria's microcolonies adorned with an extracellular matrix

NOTES FROM Q&A

Bacterial physiology, membrane dynamics, and host interactions

- The group discussed composition of the UPEC membrane and its potential impact on the growth of *E. coli*
- Data from CNA plates were discussed, which have shown effect of unfiltered spent media from *E. coli* on the growth of gram positives, suggesting a cooperative interaction between the two
- The tick's ability to assimilate fatty acids was discussed, particularly its ability to coexist with its host and potential to increase arachidonic acid levels and membrane fluidity
- Interest in studying acanthosomatid bacterial symbiosis was expressed as a way to study and reveal insights into host interactions

Urinary microbiome and epithelial response

- Interactions between two *E. coli* strains in the bladder were discussed, **highlighting need for further research on the metabolic inventory and physiological implications**
- The group discussed how different bacterial species respond variably to UTIs, with some cytotoxic to *Lactobacillus crispatus* and others not

Microbiome, ecology, and health in the bladder

- The unique niche of the bladder vs. gut was noted; lower diversity in bladder may be "normal" vs. not so in the gut
- **The potential of measuring a microbial signature in patients with BPH was discussed,** citing a paper with quantification of arachidonic acid metabolites

Recent publications Dr. Wolfe:

1. Dornbier, R. A., Doshi, C. P., Desai, S. C.... & Baldea, K. G. (2023). Metabolic syndrome and the urinary microbiome of patients undergoing percutaneous nephrolithotomy. *Asian Journal of Urology*.
2. Wolfe, A., Du, J., Khemmani, M.... & Putonti, C. (2023). Cataloging the Phylogenetic Diversity of Human Bladder Bacterial Isolates. *bioRxiv*, 2023-05.
3. James, C., Gomez, K., Desai, S.... & Wolfe, A. J. (2023). Impact of intravesical Bacillus Calmette-Guérin and chemotherapy on the bladder microbiome in patients with non-muscle invasive bladder cancer. *Frontiers in Cellular and Infection Microbiology*, *13*, 1125809.
4. Wolfe, A. J., Rademacher, D. J., Mores, C. R.... & Walker, S. J. (2023). Detection of bacteria in bladder mucosa of adult females. *The Journal of Urology*, *209*(5), 937-949.
5. Crum, E., Merchant, Z., Ene, A….& Putonti, C. (2023). Coliphages of the human urinary microbiota. *Plos one*, *18*(4), e0283930.
6. Sung, J., Larsen, P., Halverson, T. M…. & Wolfe, A. J. (2023). First trimester “clean catch” urine and vaginal swab sample distinct microbiological niches. *Microbiology Spectrum*, e02638-23.
7. Liu, F., Du, J., Lin, H.... & Feng, N. (2023). The bladder microbiome of chronic kidney disease with associations to demographics, renal function, and serum cytokines. *medRxiv*, 2023-05.
8. Cole, E. B., Khemmani, M., Liu, H.... & Shaikh, N. (2023). Urogenital urobiome of healthy children does not differ from that of children with bladder and bowel dysfunction. *Journal of Pediatric Urology*.
9. Moreland, R. B., Choi, B. I., Geaman, W.... & Wolfe, A. J. (2023). Beyond the usual suspects: emerging uropathogens in the microbiome age. *Frontiers in Urology*, *3*, 1212590.
10. Liu, F., Du, J., Lin, H.... & Feng, N. (2023). Sex-Specific Dysbiotic Bladder Microbiome in CKD Uncovered via High-Throughput Sequencing and Culture.
11. Du, J., Khemmani, M., Halverson, T... & Wolfe, A. J. (2023). Cataloging the Phylogenetic Diversity of Human Bladder Bacterial Isolates. *bioRxiv*.
12. Hilt, E., Potter, R. F., Thomas-White, K.... & Kaindl, K. (2023). Beyond the usual suspects: emerging uropathogens in the microbiome age.
13. Prasad, A., Ene, A., Jablonska, S…. & Putonti, C. (2023). Comparative Genomic Study of Streptococcus anginosus Reveals Distinct Group of Urinary Strains. *Msphere*, *8*(2), e00687-22.
14. Ene, A., Banerjee, S., Wolfe, A. J., & Putonti, C. (2023). Exploring the genotypic and phenotypic differences distinguishing Lactobacillus jensenii and Lactobacillus mulieris. *Msphere*, *8*(4), e00562-22.
15. Baddoo, G., Ene, A., Merchant, Z…. & Putonti, C. Cataloging Variation in 16S rRNA Gene Sequences of Female Urobiome Bacteria. *Frontiers in Urology*, *3*, 1270509.
16. Holthaus, E., Goodman, J., Choi, B., Khemmani, M., & Wolfe, A. J. (2023). Serial urine cultures to assess for group B strep in pregnancy. *American Journal of Obstetrics & Gynecology*, *228*(1), S462.
17. Choi, B. I., Ene, A., Du, J.... & Wolfe, A. J. (2023). Taxonomic considerations on Aerococcus urinae with proposal of subdivision into Aerococcus urinae, Aerococcus tenax sp. nov., Aerococcus mictus sp. nov., and Aerococcus loyolae sp. nov. *International Journal of Systematic and Evolutionary Microbiology*, *73*(9), 006066.
18. Liu, H., Feng, N., Wolfe, A. J., & Liu, F. (2023). Exploring Factors Affecting Acceptance of Fecal Microbiota Transplantation for Female Patients with Recurrent Urinary Tract Infections: A Descriptive Qualitative Study.
19. Brubaker, L., Chai, T. C…. & Wolfe, A. J. Tarnished Gold-the" Standard" Urine Culture: Reassessing the characteristics of a criterion standard for detecting urinary microbes. *Frontiers in Urology*, *3*, 1206046.
20. Montelongo Hernandez, C., Putonti, C., & Wolfe, A. J. (2023). Urinary Plasmids Reduce Permissivity to Coliphage Infection. *Microbiology spectrum*, *11*(4), e01309-23.
21. Brubaker, L., Horsley, H., Khasriya, R., & Wolfe, A. J. (2023). Microbiologist in the clinic: coitally related symptoms with negative urine cultures. *International Urogynecology Journal*, 1-4.
22. Halverson, T., Mueller, E. R., Brubaker, L., & Wolfe, A. J. (2023). Urobiome changes differ based on OAB treatment in adult females. *International Urogynecology Journal*, *34*(6), 1271-1277.

Recent publications from Dr. Hadjifrangiskou:

1. Bermudez, T. A., Brannon, J. R., Dudipala, N.... & Hadjifrangiskou, M. (2023). Raising the alarm: fosfomycin resistance associated with non-susceptible inner colonies imparts no fitness cost to the primary bacterial uropathogen. *Antimicrobial Agents and Chemotherapy*, e00803-23.
2. Reasoner, S. A., Flores, V., Van Horn, G.... & Hadjifrangiskou, M. (2023). Survey of the infant male urobiome and genomic analysis of Actinotignum spp. *npj Biofilms and Microbiomes*, *9*(1), 91.
3. Hadjifrangiskou, M., & Reasoner, S. (2023). Review 1:" Secretory Leukocyte Protease Inhibitor Protects Against Severe Urinary Tract Infection in Mice". *Rapid Reviews Infectious Diseases*.
4. Reasoner, S. A., Bernard, R., Waalkes, A.... & Nicholson, M. R. (2023). Longitudinal Profiling of the Intestinal Microbiome in Children with Cystic Fibrosis Treated with Elexacaftor-Tezacaftor-Ivacaftor. *medRxiv*, 2023-08.
5. Bermudez, T., Brannon, J. R., Dudipala, N.... & Hadjifrangiskou, M. (2023). Drug Resistance without a cost? Common and uncommon routes to fosfomycin resistance in Uropathogenic Escherichia coli. *bioRxiv*, 2023-06.
6. Brannon, J. R., Reasoner, S. A., Bermudez, T. A.... & Hadjifrangiskou, M. (2023). Mapping Niche-specific Two-Component System Requirements in Uropathogenic Escherichia coli. *bioRxiv*.
7. Morales, G., Abelson, B., Reasoner, S…. & Schmitz, J. (2023). The Role of Mobile Genetic Elements in Virulence Factor Carriage from Symptomatic and Asymptomatic Cases of Escherichia coli Bacteriuria. *Microbiology Spectrum*, e04710-22.
8. Hadjifrangiskou, M. (2023). Sampling the rainbow. *Nature Chemical Biology*, 1-2.
9. Flores, V., Reasoner, S., Peard, L.... & Hadjifrangiskou, M. (2023). MP70-11 DEFINING THE URINARY MICROBIOME OF THE HEALTHY INFANT BLADDER. *The Journal of Urology*, *209*(Supplement 4), e1008.
10. Hadjifrangiskou, M., Reasoner, S., Flores, V.... & Clayton, D. (2023). Defining the Infant Male Urobiome and Moving Towards Mechanisms in Urobiome Research.