



CAIRIBU UROBIOME RESEARCH INTEREST GROUP (U-RIG)

CAIRIBU U-RIG RESEARCH HOURS

EXECUTIVE SUMMARY 5/17/2024

U-RIG RESEARCH HOUR

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

DR. SIDDIQUI

“Recurrent UTI: lessons learned from the microbiome”

Challenges in diagnosing UTI due to mixed flora cultures and varying symptoms

- Growing recognition that urine is not sterile; clinical medicine struggling to keep up with the impact of the urinary microbiome on certain disorders
- Challenges in diagnosing UTIs, including mixed flora cultures and unclear symptoms
- Clinicians must consider multiple scenarios and factors when treating UTIs, including age, symptoms, and lab results

Diagnosing and managing recurrent urinary tract infections (UTIs) in various populations

- Dr. Siddiqui explained that standard urine cultures provide valuable information about the presence of microbial pathogens, host response, and other factors
 - Noted, for example, that a **middle-ground result (mixed flora) is common in older adults and females**
- However, Dr. Siddiqui cited challenges in diagnosing recurrent UTIs, particularly in older adults (30% of menopausal women have recurrent UTIs)
- **Historical dogma in microbiome sciences needs to be changed, particularly in understanding recurrent UTIs**

UTIs and their treatment, including non-antibiotic options

- Historical dogma of gut as reservoir and potential reservoirs in vagina and bladder
- Challenges in treating recurrent UTIs reflect dogma and limited evidence-based guidelines
- **Alternative approaches to preventing future UTIs needed**, e.g., non-antibiotic prophylaxis and vaginal estrogen therapy

Vaginal estrogen's impact on the female microbiome during aging and menopause

- Dr. Siddiqui explained the importance of vaginal estrogen therapy for recurrent UTIs in peri/postmenopausal women
- Discussed impact of aging and menopause on the female microbiome, including recurrent UTIs
- Discussed dominance of Lactobacilli in vagina and urinary bladder, with a drop in abundance post-menopause and recovery with estrogen therapy
- **Vaginal estrogen use, even at low levels, has led to higher Lactobacillus abundance in postmenopausal women**

Lactobacillus in UTI, including abundance and species-level resolution

- Researchers found that postmenopausal women with rUTI had more Lactobacilli in urine, despite daily antibiotics



CAIRIBU U-RIG RESEARCH HOUR BRIDGING KNOWLEDGE GAPS IN THE UROBIOME





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Chelsie Armbruster, PhD
Associate Professor
Department of Microbiology and Immunology
State University of New York at Buffalo

SPEAKERS

FRIDAY, MAY 17
3:00 PM ET
2 PM CENTRAL | 12 PM PACIFIC



- Discussed Lactobacillus in the microbiome, including mechanisms of action and species-level resolution
 - Study found same species in urinary and vaginal niches from same individuals, with prevalence of crispatus, gasseri, inners, and jensenii

Improving UTI diagnosis, treatment, and prevention

- Dr. Siddiqui stressed importance of estrogen in treating UTIs, **yet poor uptake in clinical setting**
- Noted that patients are more likely to use a therapy when they understand why it works – UTIs are no exception
- Highlighted importance of considering the microbiome in UTI diagnosis and treatment
- Suggested pairing vaginal estrogen with probiotic for bladder health

UTI in long-term catheterized individuals, focusing on microbiome composition and stability

- Highlighted effects on urinary microbiome of long-term urinary catheterization, noting role of urea-splitting bacteria (e.g., *Proteus Mirabilis*)
- In long-term care facilities, colonization by multi-drug resistant organisms complicates effective treatment of UTI
- Dr. Siddiqui concluded by sharing that her research aims to better understand composition and consequences of polymicrobial bacteriuria in catheterized individuals, including stability of the microbiota and impact of perturbations such as catheter changes and antibiotic use

DR. ARMBRUSTER

“Composition and consequences of polymicrobial bacteriuria during long-term catheterization”

UTIs in long-term catheterized individuals

- Dr. Armbruster presented prospective longitudinal data from study on 50 individuals with long-term catheters
- Presented culture results from urine specimens, which showed **high prevalence of poly-microbial infections (97%) with >10 colony-forming units**
- Long-term catheterized individuals in nursing homes and outpatient settings had similar microbial profiles, averaging 3-4 species per sample

UTIs in long-term catheterized patients, including colonization and symptoms

- Dr. Armbruster has found that **catheter changes and antibiotics can alter urinary microbiome in patients**
- She examined urine cultures and urinalysis results among long-term catheterized individuals, which revealed challenges in distinguishing asymptomatic colonization from active infections

UTI diagnosis and treatment challenges, focus on microbial interactions and implications for disease severity

- Highlighted issues with diagnosis in patients with persistent asymptomatic colonization
- Studies in mouse models and with genomic analyses have shown how microbial interactions influence risk and severity of catheter-associated UTIs

Optimizing microbial DNA extraction methods for urine samples with diverse microbes

- **Challenges in analyzing urine samples from catheterized patients include high levels of host material and biofilms**
- Optimized methods for extracting microbial DNA and reducing false DNA are needed, including in scenario of host cell lysis and depletion of extracellular DNA
- Has used QIAGEN, kya, amp, and zymo kits to analyze urine samples, with varying results
 - Zymo kit provided the closest approximation to the expected microbial composition, with overrepresentation of *Pseudomonas*
- Dr. Armbruster discussed her research on the persistence of a single strain of bacteria in a patient for six months, picking up snips that changed its pathogenesis

*****BELOW are recent publications from Dr. Siddiqui and Dr. Armbruster*****

Recent publications from Dr. Siddiqui (2022 through the present)

1. Advani SD, Claeys KC, **Siddiqui NY**. What Should I Know About Recurrent UTIs in Older Women? JAMA Intern Med. 2024. doi:10.1001/jamainternmed.2024.1854.
2. Jiang D, Soo N, Tan CY, Dankwa S, Wang HY, Theriot BS, Ardeshir A, **Siddiqui NY**, Van Rompay KKA, De Paris K, Permar SR, Goswami R, Surana NK. Commensal bacteria inhibit viral infections via a tryptophan metabolite. Preprint. bioRxiv. 2024;2024.04.21.589969. doi:10.1101/2024.04.21.589969.
3. Advani SD, Turner NA, North R, Moehring RW, Vaughn VM, Scales Jr CD, **Siddiqui NY**, Schmader KE, Anderson DJ. Proposing the "Continuum of UTI" for a Nuanced Approach to Diagnosis and Management of Urinary Tract Infections. J Urol. 2024;211(5):690-698. doi:10.1097/JU.0000000000003874.
4. London LY, Lim CH, Modliszewski JL, **Siddiqui NY**, Sysoeva TA. Draft genomes of Lactobacillus delbrueckii and Klebsiella pneumoniae coexisting within a female urinary bladder. Microbiol Resour Announc. 2023;12(10). doi:10.1128/MRA.00305-23.
5. O'Shea M, **Siddiqui NY**, Truong T, Erkanli A, Barber MD. Standard Restrictions vs Expedited Activity After Pelvic Organ Prolapse Surgery: A Randomized Clinical Trial. JAMA Surg. 2023;158(8):797-805. doi:10.1001/jamasurg.2023.1649.
6. O'Shea M, Routh JC, **Siddiqui NY**. Robot-assisted laparoscopic anterior urethral diverticulectomy. Int Urogynecol J. 2023;34(2):589-592. doi: 10.1007/s00192-022-05355-7.
7. O'Shea M, Boyles S, Bradley CS, Jacobs K, McFatrigh M, Sung V, Weinfurt K, **Siddiqui NY**. AUGS-PERFORM: A New Patient-Reported Outcome Measure to Assess Quality of Prolapse Care. Female Pelvic Med Reconstr Surg. 2022;28(8):468-478. doi:10.1097/SPV.0000000000001225.
8. Kowalski JT, Wiseman JB, Smith AR, Helmuth ME, Cameron A, DeLancey JOL, Hendrickson WK, Jelovsek JE, Kirby A, Kreder K, Lai HH, Mueller M, **Siddiqui NY**, Bradley CS. Natural history of lower urinary tract symptoms in treatment-seeking women with pelvic organ prolapse; the Symptoms of Lower Urinary Tract Dysfunction Research Network (LURN). Am J Obstet Gynecol. 2022;227(6):875.e1-875.e12. doi:10.1016/j.ajog.2022.07.038.
9. **Siddiqui NY**, Ma L, Brubaker L, Mao J, Hoffman C, Dahl EM, Wang Z, Karstens L. Updating Urinary Microbiome Analyses to Enhance Biologic Interpretation. Front Cell Infect Microbiol. 2022;12:789439. doi:10.3389/fcimb.2022.789439.
10. Johnson JA, Delaney LF, Ojha V, Rudraraju M, Hintze KR, **Siddiqui NY**, Sysoeva TA. Commensal Urinary Lactobacilli Inhibit Major Uropathogens In Vitro With Heterogeneity at Species and Strain Level. Front Cell Infect Microbiol. 2022;12:870603. doi:10.3389/fcimb.2022.870603.
11. Vaughan MH, Zemtsov GE, Dahl EM, Karstens L, Ma L, **Siddiqui NY**. Concordance of urinary microbiota detected by 16S ribosomal RNA amplicon sequencing vs expanded quantitative urine culture. Am J Obstet Gynecol. 2022;227(5):773-775. doi:10.1016/j.ajog.2022.06.031.
12. Luchristt D, Meekins AR, Zhao C, Grotegut C, **Siddiqui NY**, Alhanti B, Jelovsek JE. Risk of obstetric anal sphincter injuries at the time of admission for delivery: A clinical prediction model. BJOG. 2022;129(12):2062-2069. doi:10.1111/1471-0528.17239.
13. Luchristt D, **Siddiqui NY**, Bretschneider CE, Jelovsek JE. Quantifying the Added Value of 2 Common Frailty Measures for Predicting Adverse Outcomes After Elective Hysterectomy. Urogynecology (Phila). 2022;28(8):526-532. doi:10.1097/SPV.0000000000001198.
14. Johnson JA, Modliszewski JL, **Siddiqui NY**, Sysoeva TA. Draft Genome Sequence of a Lactobacillus gasseri Strain Isolated from the Catheterized Urine of a Healthy Postmenopausal Woman. Microbiol Resour Announc. 2022;11(6). doi:10.1128/mra.00021-22.
15. Luchristt D, Weidner AC, **Siddiqui NY**. Urinary basement membrane graft-augmented sacrospinous ligament suspension: a description of technique and short-term outcomes. Int Urogynecol J. 2022;33(5):1347-1350. doi:10.1007/s00192-022-05159-9.
16. Hendrickson WK, Havrilesky L, **Siddiqui NY**. Cost-effectiveness of bacteriuria screening before urogynecologic surgery. Am J Obstet Gynecol. 2022;226(6):831.e1-831.e12. doi:10.1016/j.ajog.2021.11.1375.

Recent publications from Dr. Armbruster (2021 through the present)

1. Johnson AO, Shipman BM, Hunt BC, Learman BS, Brauer AL, Zhou SP, Blair RH, De Nisco NJ, **Armbruster CE**. Function and contribution of two putative Enterococcus faecalis glycosaminoglycan degrading enzymes to bacteremia and catheter-associated urinary tract infection. bioRxiv [Preprint]. 2024;2024.05.08.593205. doi:10.1101/2024.05.08.593205.
2. Evstafeva D, Ilievski F, Bao Y, Luo Z, Abramovic B, Kang S, Steur C, Montanari E, Casalini T, Simicic D, Sessa D, Mitrea SO, Pierzchala K, Cudalbu C, **Armbruster CE**, Leroux JC. Inhibition of urease-mediated ammonia production by 2-octynohydroxamic acid in hepatic encephalopathy. Nat Commun. 2024;15(1):2226. doi:10.1038/s41467-024-46481-8.
3. Johnson AO, Shipman BM, Hunt BC, Learman BS, Brauer AL, Zhou SP, Hageman Blair R, De Nisco NJ, **Armbruster CE**. Function and contribution of two putative Enterococcus faecalis glycosaminoglycan degrading enzymes to bacteremia and catheter-associated urinary tract infection. Infect Immun. Published online June 6, 2024. doi:10.1128/iai.00199-24.
4. Brauer AL, Learman BS, **Armbruster CE**. Differential Contribution of Hydrogen Metabolism to Proteus mirabilis Fitness during Single-Species and Polymicrobial Catheterized Urinary Tract Infection. Pathogens. 2023;12(12):1377.

5. Hunt BC, Brix V, Vath J, Guterman BL, Taddei SM, Learman BS, Brauer AL, Shen S, Qu J, **Armbruster CE**. Metabolic interplay between *Proteus mirabilis* and *Enterococcus faecalis* facilitates polymicrobial biofilm formation and invasive disease. *bioRxiv* [Preprint]. 2024;2023.03.17.533237. doi:10.1101/2023.03.17.533237.
6. Herout R, Khoddami S, Moskalev I, Reicherz A, Chew BH, **Armbruster CE**, Lange D. Role of Bacterial Surface Components in the Pathogenicity of *Proteus mirabilis* in a Murine Model of Catheter-Associated Urinary Tract Infection. *Pathogens*. 2023;12(4):509. doi:10.3390/pathogens12040509.
7. Brauer AL, Learman BS, **Armbruster CE**. Differential contribution of hydrogen metabolism to *proteus mirabilis* fitness during single-species and polymicrobial catheterized urinary tract infection. *Pathogens*. 2023;12(2):1377. doi:10.3390/pathogens12121377.
8. **Armbruster CE**, França Â, Kushugulova A, Mauch RM, Martín-Rodríguez AJ. Editorial: Rising stars in biofilms 2022. *Front Cell Infect Microbiol*. 2023;13:1169998. doi:10.3389/fcimb.2023.1169998.
9. Brauer AL, Learman BS, Taddei SM, Deka N, Hunt BC, **Armbruster CE**. Preferential catabolism of l- vs d-serine by *Proteus mirabilis* contributes to pathogenesis and catheter-associated urinary tract infection. *Mol Microbiol*. 2022;118(3):125-144. doi:10.1111/mmi.14968.
10. White AN, Learman BS, Brauer AL, **Armbruster CE**. Catalase Activity is Critical for *Proteus mirabilis* Biofilm Development, Extracellular Polymeric Substance Composition, and Dissemination during Catheter-Associated Urinary Tract Infection. *Infect Immun*. 2021;89(10). doi:10.1128/IAI.00177-21.
11. **Armbruster CE**. mSphere of Influence: Of Mice, Men, and Microbes-How Well Do Experimental Models Recapitulate Human Infection? *mSphere*. 2021;6(2). doi:10.1128/mSphere.00228-21.
12. Gaston JR, Johnson AO, Bair KL, White AN, **Armbruster CE**. Polymicrobial interactions in the urinary tract: is the enemy of my enemy my friend? *Infect Immun*. 2021; IAI.00652-20. doi:10.1128/IAI.00652-20.
13. **Armbruster CE**, Brauer AL, Humby MS, Shao J, Chakraborty S. Prospective assessment of catheter-associated bacteriuria clinical presentation, epidemiology, and colonization dynamics in nursing home residents. *JCI Insight*. 2021;6(19). doi:10.1172/jci.insight.144775.