



CAIRIBU UROBIOME RESEARCH INTEREST GROUP (U-RIG)

CAIRIBU U-RIG RESEARCH HOURS

EXECUTIVE SUMMARY 4/19/2024 U-RIG RESEARCH HOUR

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

DR. SCHREIBER

*Urinary tract infections, focusing on lower urinary tract infection caused by *E. coli**

- UTIs affect millions annually, with \$12B in treatment expenditure and 15% of antibiotic prescriptions dedicated to UTIs, disproportionately affecting women
- Dr. Henry Schreiber discussed his research on the gut-bladder axis with a focus on a clinical sampling collection
- He highlighted contributions of Colin Warby and Mark Young at the Earl Lab at the Broad Institute, who were major drivers of the collaboration

****E. coli* colonization in gut, bladder, and vagina reservoirs impact UTIs***

- UTIs recur due to persistence of bacterial strains in an uninfected reservoir within the body
- Dr. Schreiber highlighted 4 areas *E. coli* can inhabit, including gut, bladder, vagina, and periurethral area
- He is investigating interactions between *E. coli*, microbiome, and host immunity in susceptibility to UTI

Gut-bladder connection in UTIs, with focus on persistence of pathogens in gut after antibiotic

- Collected fecal and urine samples from 28 women with varying infection histories
- Hypothesized that gut and bladder strains may be genetically distinct in populations with UTIs
- Found that *E. coli* strains in gut persisted after UTI treatment, even after antibiotics
- Sexual intercourse may contribute to gut *E. coli* translocation and UTI risk, study suggested

Gut *E. coli* populations in urinary tract infections

- Found that B2/D strains of *E. coli* were more frequent in the gut and urine of women with h/o UTIs vs. control
- **But despite differences in gut microbiome abundance, the same B2/D strains were found in both cohorts**
- Women with rUTI had lower gut microbiota diversity than control women

Gut microbiome differences between UTI and control groups

- Discussed relationship between antibiotic use and microbial diversity in patients with h/o UTI. While those with UTI consumed more antibiotics than controls, there was no clear correlation between antibiotic use and microbial diversity within patient samples.
- Found higher taxonomic levels for certain bacteria, such as Bacteroidaceae and Ruminococcaceae, but limited power to capture species-level differences due to small sample size
- Reduction in butyrate producers in UTI gut microbiomes may contribute to inflammation
- **Correlation analysis revealed similarities between UTI and IBD gut microbiomes, despite differences in diversity and short chain fatty acids**



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



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SPEAKERS

FRIDAY, APRIL 19
3:00 PM ET
2 PM CENTRAL | 12 PM PACIFIC



Gut dysbiosis and immune response in women with recurrent urinary tract infections

- Women with recurrent UTIs had gut microbiome dysbiosis, with distinct composition and metabolomic profiles
- Immune system profile phenotypes in women with rUTI are mild, but statistically significant, with upregulation of eotaxin cytokine II, associated with eosinophil recruitment and bladder inflammation
- Dr. Schreiber discussed dysbiosis and immune response in UTI; preliminary data suggest impact on outcomes
- Despite lack of change in gut microbiome population dynamics, Dr. Schreiber explored for connection between gut dysbiosis and increased uropathogen colonization in bladder

E. coli gene expression differences in urinary tract infections

- He described a method for amplifying low-abundance *E. coli* strains in a complex community using hybrid selection – ***E. coli PanSelect*** (reach out to [Ashlee Earl](#), Research Scientist, Director of the Bacterial Genomics Group, Institute Scientist, Broad Institute if interested in this system)
- The method showed unbiased amplification of DNA and RNA molecules from non-detected strains, allowing for strain-level identification and gene expression analysis
- Dr. Schreiber's results showed difference in *E. coli* life cycle between UTI and control groups, with upregulation of RNA genes in UTI group
- FNR and RNA regulation are key in rUTI, with de-repression (by ArcA) of aerobic machinery and lower activation of FNR-controlled genes. Indicates that strains are responding as if they are in an environment with increased aerobic respiration potential
- *E. coli* in UTI gut microbiome showed higher aerobic and nitrate-based respiration

E. coli adaptation in gut and bladder environments

- Dr. Schreiber suggested that *E. coli* may better adapt to anaerobic metabolism due to exposure to mild inflammatory environment in rUTI gut microbiota
- Questioned whether *E. coli* strains are better at transitioning from gut to aerobic environment or if environmental factors play a larger role
- Dr. Schreiber concluded by discussing the lack of evidence for antibiotic resistance in individuals with UTIs while also raising the possibility of bladder epithelial changes supporting a specific bacterial clade

Recent publications Dr. Schreiber:

1. Young MG, Straub TJ, Worby CJ, et al. Distinct *Escherichia coli* transcriptional profiles in the guts of recurrent UTI sufferers revealed by pan-genome hybrid selection. Preprint. bioRxiv. 2024;2024.02.29.582780; doi:10.1101/2024.02.29.582780.
2. Worby CJ, **Schreiber HL**, Straub TJ, et al. Longitudinal multi-omics analyses link gut microbiome dysbiosis with recurrent urinary tract infections in women. *Nat Microbiol.* 2022;7(5):630-639. doi:10.1038/s41564-022-01107-x.
3. Van Dijk LR, Walker BJ, Straub TJ, et al. StrainGE: a toolkit to track and characterize low-abundance strains in complex microbial communities. *Genome Biol.* 2022;23(1):74. doi:10.1186/s13059-022-02630-0.
4. Straub TJ, Chou WC, Manson AL, **et al.** Limited effects of long-term daily cranberry consumption on the gut microbiome in a placebo-controlled study of women with recurrent urinary tract infections. *BMC Microbiol.* 2021;21(1):53. doi:10.1186/s12866-021-02106-4.
5. Morais LH, **Schreiber HL**, Mazmanian SK. The gut microbiota-brain axis in behaviour and brain disorders. *Nat Rev Microbiol.* 2021;19(4):241-255. doi:10.1038/s41579-020-00460-0.
6. Spaulding CN, Klein RD, **Schreiber HL**, et al. Precision antimicrobial therapeutics: the path of least resistance?. *NPJ Biofilms Microbiomes.* 2018;4:4. doi:10.1038/s41522-018-0048-3.
7. Spaulding CN, **Schreiber HL**, Zheng W, et al. Functional role of the type 1 pilus rod structure in mediating host-pathogen interactions. *Elife.* 2018;7:e31662. doi:10.7554/eLife.31662.
8. Paharik AE, **Schreiber HL**, Spaulding CN, et al. Narrowing the spectrum: the new frontier of precision antimicrobials. *Genome Med.* 2017;9(1):110. doi:10.1186/s13073-017-0504-3.
9. Walker JN, Flores-Mireles AL, Pinkner CL, et al. Catheterization alters bladder ecology to potentiate *Staphylococcus aureus* infection of the urinary tract. *Proc Natl Acad Sci U S A.* 2017;114(41):E8721-E8730. doi:10.1073/pnas.1707572114.