# National Institutes of Health

# National Institute of Diabetes and Digestive and Kidney Diseases

# Collaborating for the Advancement of Interdisciplinary Research in Benign Urology

# Annual Meeting

# In-person Meeting

# November 30–December 2, 2022

# DRAFT EXECUTIVE SUMMARY

## Overview of the Meeting

The purpose of the [Collaborating for the Advancement of Interdisciplinary Research in Benign Urology (CAIRIBU) Annual Meeting](https://www.niddk.nih.gov/news/meetings-workshops/2022/cairibu-2022-annual-meeting) is to bring together the Directors and research teams of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) U54 O’Brien Urology Centers, P20 Exploratory Centers for Interdisciplinary Research in Benign Urology, and Multidisciplinary K12 Urologic Research (KURe) and Urological Epidemiology (KEpi) Institutional Research Career Development Programs. Collectively, these Centers and Programs fall under the [CAIRIBU](https://cairibu.urology.wisc.edu/) umbrella.

The annual meeting encourages the exchange of scientific knowledge about advances in benign genitourinary (GU) research and provides a platform for building interactions among CAIRIBU Centers and Programs, as well as among CAIRIBU investigators and the broader benign urologic research community. The primary objectives of the meeting were to (1) share research resources and (2) advance students and early stage investigators in their development as future leaders in the field of benign urology.

The meeting agenda included [five scientific sessions](https://www.youtube.com/@cairibu3315), two keynote lectures, three poster sessions, and two networking and interactions sessions. The interactive poster sessions featured the work of trainees and early stage investigators whose abstracts were selected for presentation.

## Keynote Lectures

*Speakers:* *Kevin McVary, M.D., Loyola University Medical Center*

Geolani Dy, M.D., Oregon Health & Science University

Dr. Kevin McVary outlined progress in and challenges to employing translational science to manage lower urinary tract symptoms (LUTS) and benign prostatic hyperplasia (BPH). The worldwide impact of BPH/LUTS is rising; associated health care costs are increasing, and the current clinical workforce is insufficient to meet the growing needs for health care. Attention to preventive, complementary, and cost‑effective treatment strategies for BPH/LUTS will be crucial. Numerous factors (e.g., association with obesity) must be considered when diagnosing and treating benign GU conditions, and several pathophysiologic mechanisms are at play. Many opportunities exist to address unmet needs in this area. Dr. McVary emphasized that perspectives from specialists of multiple disciplines often are necessary to understand the full picture of disease. He also reflected on opportunities for translational science team–building and mentorship within the CAIRIBU community, as well as the need for sustained investment and engagement in this area.

Dr. Geolani Dy spoke on building a gender-affirming surgery (GAS) research agenda, with a focus on community engagement and patient-centered outcomes research. The Transgender and Nonbinary Surgery Allied Research Collective (TRANS ARC) is working to identify gaps in GAS research through patient-centered outcomes. TRANS ARC’s initial goals were to recruit a multistakeholder perspective, host a summit, and develop prioritized research questions. Challenges were related to cultural, geographic, and health system contexts; institutional hurdles; and building trust. Dr. Dy explained that a trauma-informed approach is key. She also highlighted the development of the Transgender and Nonbinary Surgery Patient-Reported Outcomes registry, which addresses community researcher and surgeon-researcher goals. Key takeaways from community partners were related to social determinants of health, implementation, sexuality, and data privacy. Taken together, these efforts will help address long-term outcomes, shared decision-making, transparency, and development of interventions. Long-term goals focus on cultural changes, quality of research, information sharing, patient experiences, surgical practices, and access to care.

## Scientific Sessions

### Scientific Session 1: LUTS/Lower Urinary Tract Dysfunction and Prostate

Moderators: Marvin Langston, Ph.D., M.P.H., Stanford University, University of California, San Francisco (UCSF)–Kaiser Permanente (KUroEpi)

Hannah Miles, University of Wisconsin–Madison (UW–Madison) (U54)

Speakers: Scott Bauer, M.D., Sc.M., UCSF–Kaiser Permanente (KUroEpi), UW–Madison (U54)

Petra Popovics, Ph.D., Eastern Virginia Medical School, UW–Madison (KURe)

Jonathan Pollack, M.D., Ph.D., Stanford University (U54)

Doug Strand, Ph.D., The University of Texas Southwestern Medical Center, UW–Madison (U54)

Chad Vezina, Ph.D., UW–Madison (U54)

Jill Macoska, Ph.D., University of Massachusetts Boston, UW–Madison (U54)

Shane Wells, M.D., UW–Madison (U54)

Dr. Scott Bauer presented on defining and targeting aging mechanisms of urinary symptoms in older men, with a focus on mitochondria. His research mission is to help treat older adults with LUTS by studying how aging cells, tissues, organs, and systems contribute to common urologic symptoms. Age-related changes in the GU tract often do not meaningfully increase the risk of clinical outcomes, and more accurate measures and new targets are needed. Dr. Bauer explained how age-related LUTS reflects aspects of biological, phenotypic, and functional aging. He is applying this framework in the context of mitochondrial disease. His results indicate an unexpected relationship between citrate synthase activity with BPH, which underscores the need for further work in this area.

Dr. Petra Popovics spoke on recent progress and future directions in investigating the prostate immune landscape. Her research is focused on chronic inflammation and pathological processes in BPH/LUTS. Using a mouse model of BPH, she identified a mechanism by which foam cells infiltrate the lumen in the ventral mouse prostate, potentially leading to urinary dysfunction. Future questions relate to the origin of luminal macrophages, the role of foam cells in BPH pathology, drivers of the translocation of macrophages to the lumen, and lipid accumulation in association with BPH. Future studies will explore the association of prostate immune remodeling with comorbid factors.

Dr. Jonathan Pollack discussed genomic insights into BPH pathogenesis. Several key features of BPH have been described, but many of the cellular and molecular pathways that underlie BPH are poorly understood. Dr. Pollack uses genomic approaches to survey BPH tissues. His analysis indicates a potential role of *CXCL13* in BPH. *CXCL13* expression associates with lymphocyte infiltrates, and lymphoid aggregates have been observed in BPH. His findings suggest that a specific adaptive T-cell response might play a role in BPH pathogenesis. Ongoing and future studies will identify drivers, validate T-cell oligoclonality, define relevant T-cell subset phenotypes, identify the microbial or self-antigens, and explore new therapeutic avenues.

Dr. Doug Strand spoke on tissue and data resources for human lower urinary tract research. His research is focused on the anatomy and cellular pathogenesis of lower urinary tract dysfunction. Using single-cell RNA sequencing, he identified novel cell types in the prostatic urethra. These data provide new insights into the hierarchical definition of human prostate cell types; work on this area is ongoing. Future plans include generating multi-ome data from the lower urinary tract across aging, ethnicity, and disease; creating a browsable database of clinically annotated tissue specimens; and developing new lineage tracer models.

Dr. Chad Vezina discussed his work using a molecular approach to trace the cell lineage responsible for prostate fibrosis. He is interested in further characterizing the interplay between collagen formation and LUTS in men. Dr. Vezina is tracing cell lineages through prostate infection to characterize cell types that might give rise to collagen formation. He found that bone marrow–derived myeloid cells are recruited to the inflamed prostate and produce collagen. Several lineages were found to contribute to collagen-producing cells in the inflamed prostate, and many of the genes are co-expressed in the same cells. His results indicate that *CCR2* plays a critical role in this process.

Dr. Jill Macoska outlined fibroblast plasticity in the lower urinary tract. The prostate microenvironment can be modulated through various biological processes, including metabolic syndrome, inflammation, aging, diabetes, and obesity. These processes (i.e., “inflammaging”) alter microenvironmental niches by promoting cellular senescence and can induce fibroblast plasticity. The senescence-associated secretory phenotype promotes fibrosis. Dr. Macoska found that prostate fibroblasts from older men are likely to secrete inflammatory mediators that promote collagen accumulation in the extracellular matrix. She hypothesized that activation of the IL-4 and IL-13 axis pushes the prostate fibroblasts to adopt a hybrid fibroblast/immune cell phenotype, potentially suppressing apoptosis and leading to fibrotic persistence.

Dr. Shane Wells spoke about his collaborative research on image-based biomarkers for the prostate and lower urinary tract. He began by describing parallels between the development of liver elastography to non-invasively monitor liver fibrosis and the potential for diagnosing and monitoring prostate fibrosis. He emphasized the importance of quantitative imaging techniques. Dr. Wells described how advanced imaging techniques, such as magnetic resonance elastography (MRE), shear wave elastography (SWE), and Uro-Dynamic MRI can provide insight into prostate stiffness and the effect on voiding dynamics in patients with and without BPH. He emphasized the need to better understand metabolic risk factors for BPH; quantitative techniques can be valuable for this effort as well.

### Scientific Session 2: GU Microbes and Infection

Moderators: Teresa Liu, Ph.D., UW–Madison (U54)

Grace Morales, Vanderbilt University (P20)

Speakers: Nicholas Steers, Ph.D., Columbia University (U54)

Maryellen Kelly, D.N.P., Ph.D., M.H.S., Duke University (KURe)

Miguel Verbitsky, Ph.D., Columbia University (U54)

Seth Reasoner, Vanderbilt University (P20)

Maria Hadjifrangiskou, Ph.D., Vanderbilt University (P20)

*Tanya Sysoeva, Ph.D., The University of Alabama in Huntsville, Duke University (KURe)*

Jonathan Barasch, M.D., Ph.D., Columbia University (U54)

Dr. Nicholas Steers discussed his work on resident and recruited macrophages in bladder health and disease. Resident macrophages help maintain homeostatic functions across organs, but these dynamics have been relatively understudied in the bladder. Dr. Steers developed a deep-phenotyping panel to examine macrophage populations in a mouse model. Using multiparameter flow cytometry, he is identifying unique macrophage populations in the steady state and in response to urinary tract infection (UTI). This approach can be used to isolate specific populations for transcriptomic analysis and functional studies to determine the role that the populations play in tissue homeostasis and the immune response. Lineage tracing can provide additional information on the sources of macrophage populations.

Dr. Maryellen Kelly presented her work on the pediatric urinary microbiome at species-level resolution. She explained that studies of the urinary microbiome in children can provide insight into the development of the microbiome over time. She evaluated microbiome presence and composition in catharized urine of children and found differences in the urinary microbiome composition with age and between sexes. Dr. Kelly currently is comparing the urinary microbiome in pilot cohorts of children with and without recurrent UTI. She also is determining the stability of the pediatric urinary microbiome over time.

Dr. Miguel Verbitsky discussed his research on urine microbiota analysis and microbiota genome-wide association studies (GWAS) in children with UTI and vesicoureteral reflux. He hypothesized that host clinical variables and genetic factors are associated with specific urinary microbiota profiles, possibly because they predispose the host to a specific anatomic defect that factors certain taxa or affects immunity. Top polymorphisms were on or near genes associated with immune surveillance, inflammation, and GU tract development and disease. Dr. Verbitsky also tested associations of polymorphisms with multiple phenotypes. The top association was with coronary disease; other possible associations include postoperative infection, functional diseases of the bladder, urinary obstruction, and UTI.

Mr. Seth Reasoner described methods for detecting the infant urinary microbiome, which reflects numerous developmental factors and plays a role in the development of the immune system and susceptibility to disease in the future. Actinotignum schaalii, an opportunistic pathogen associated with UTI, was the most common species detected. Whole-genome sequencing revealed insights into potential interactions with other microbes. Future directions include providing analysis codes and a urinary microbiome analysis tutorial to the public, as well as monitoring the development of the urinary microbiome during childhood.

Dr. Maria Hadjifrangiskou explained how uropathogenic Escherichia coli (UPEC) subverts mitochondrial metabolism to enable intracellular bacterial pathogenesis in UTI. She is interested in understanding intracellular bacterial expansion, as well as the stress imposed on the host cell during bacterial replication. UPEC biofilms have distinct spatial organization as a function of oxygen gradients. Dr. Hadjifrangiskou is interested in determining which enzyme complexes are used within the host cell. Using a mouse model for UTI, she showed that bacteria consume oxygen during intracellular infection. She is interested in better understanding the dynamics of these interactions. In the model, she observed that in stabilized hypoxia-inducible factor 1 controlled the shift to glycolysis, possibly preventing apoptosis.

Dr. Tanya Sysoeva presented on the role of a virulence factor, TraT, that is ubiquitous in drug-resistant UPEC. She explained that drug resistance is spread primarily by gene transfer and plasmid conjugation. Mechanisms for natural conjugation inhibition, however, are in place. Dr. Sysoeva is interested in applying this mechanism to prevent drug resistance. TraT could serve as a multifunctional protector, but the mechanisms of this protection are unknown. Using size-exclusion chromatography, she found that the TraT domain forms mixed oligomers in solution. Additionally, the soluble TraT domain protects sensitive E. coli cells. She currently is examining the role of TraT in UPEC serum resistance.

Dr. Jonathan Barasch discussed hematuria, heme metabolism, and UTI. Iron is required for bacterial replication, and many environments are deficient in iron. As a result, infection increases urinary host iron, as well as heme-associated proteins. Sex- and time-dependent differences are present in these effects. Dr. Barasch’s research has demonstrated that urothelia must metabolize heme for survival, and he has identified genes involved in the pathways. The bladder epithelium is metabolically active and deactivates heme, but this process could result in cellular death.

### Scientific Session 3: Bladder Physiology and Function

Moderator: Cindy Amundsen, M.D., Duke University (KURe)

Byron Hayes, Ph.D., Duke University (KURe)

Speakers: Cathy Mendelsohn, Ph.D., Columbia University (U54)

Ali Gharavi, M.D., Columbia University (U54)

Eli Broemer, Michigan State University, Oakland University William Beaumont School of Medicine (P20)

Michael Odom, Ph.D., D*uke University (KURe)*

Indira Mysorekar, Ph.D., Baylor College of Medicine, Washington University (P20)

Dr. Cathy Mendelsohn discussed transcriptional control of urothelial specification in homeostasis and regeneration. She is interested in activation of basal cells in response to injury from UTI, carcinogens, and chemicals. Peroxisome proliferator–activated receptor gamma (Pparg) is a transcription factor that induces the differentiation of basal cells into superficial cells. Dr. Mendelsohn tested the use of Pparg agonist to treat basal or squamous tumors or restore normal differentiation in the bladder. She found that the treatment induces apoptosis of basal tumors and exit from the cell cycle. Next steps will involve exploring this topic further using models for disease.

Dr. Ali Gharavi spoke on opportunities for genomic medicine in benign urology. Genome sequencing has become more cost-effective in recent years, and can be used for identifying rare and common variants that can predict an individual’s risk of disease. This capability has not been explored fully in the context of benign urology. Dr. Gharavi described case studies of patients presenting with symptoms indicating congenital kidney disorders and highlighted common microdeletion syndromes that have been observed in clinical practice. An interplay exists between several benign adult onset GU phenotypes such as BPH and developmental pathways. He noted that biorepositories now enable analysis of a wide variety of traits and can empower benign urology research.

Mr. Eli Broemer presented on 3-D reconstruction during *ex vivo* filling and insights into bladder biomechanics. Traditionally, mechanics of bladder filling have been measured by dissecting and stretching the tissue square. Mr. Broemer described an alternative method, which involves filling the intact *ex vivo* bladder, measuring internal pressure, and analyzing the 3-D space. Using mouse bladder tissue, he reconstructed 3-D bladder volumes. He used spatial carving to reconstruct the 3-D image and then generated a 4-D image using meshing. Mr. Broemer then used spherical and elliptical analysis to calculate wall stretch and stress. Studies in mouse and other animal models indicate that the bladder undergoes anisotropic behavior during filling.

Dr. Michael Odom discussed his work on detrusor contractility via prostaglandin F (FP) receptor activation using diabetic mice with bladder underactivity. The NLRP3 inflammasome causes urothelial pyroptosis and is activated by diabetic metabolites. He is using a novel genetic mouse model to determine NLRP3-dependent signaling pathways responsible for bladder contractility that are dysregulated by diabetes. His results indicate that NLRP3 inflammation dysregulates prostaglandin signaling. FP receptor agonists could be effective therapeutics for underactive diabetic bladder dysfunction. Future directions include investigating FP receptor populations, second-messenger systems, and bladder function *in vivo*.

Dr. Indira Mysorekar spoke on mechanisms and interventions related to the effects of aging on urothelial homeostasis. She uses a mouse model to understand how the bladder changes with age at homeostasis and in the context of various diseases. Dr. Mysorekar is interested in studying autophagy and lysosomal function in the aged bladder. Aged bladders exhibit elevated senescence and cellular damage pathways, indicating chronic stress. Antioxidant response deficiency also has been observed. Epithelial aging results in pyroptotic cell death leading to impaired barrier function. Dr. Mysorekar explained that D-mannose ameliorates these age-associated effects and could be a useful senomorphic drug for older patients.

### Scientific Session 4: Bladder and Neurourology

Moderators: *Bernadette Zwaans, Ph.D., Oakland University William Beaumont School of Medicine (P20)*

*Sarah Bartolone, Oakland University William Beaumont School of Medicine (P20)*

Speakers: Pragya Saxena, Michigan State University, Oakland University William Beaumont School of Medicine (P20)

B. Malique Jones, Michigan State University, Oakland University William Beaumont School of Medicine (P20)

Ramy Goueli, M.D., The University of Texas Southwestern Medical Center

LaTasha Crawford, V.M.D., Ph.D., DACVP, UW–Madison (KURe)

Kimberly Keil Stietz, Ph.D., UW–Madison (U54), Stanford University (U54)

Alison Huang, M.D., UCSF–Kaiser Permanente (KUroEpi)

Ms. Pragya Saxena spoke on the mechanism of increased detrusor contractility induced by mast cell activator compound 48/80 in the murine urinary bladder. She explained that the rate of rise of pressure events is vital to sensory outflow. In particular, she is interested in wall stiffness and elasticity, which influence proper filling and voiding and wall compliance. Ms. Saxena is collecting video recordings of *ex vivo* filling. She is studying how mast cell activation alters compliance. She proposed a potential mechanism in which compound 48/80 acts on mast cells, leading to increased compliance. Future studies involve further exploration of matrix metalloproteinases and prostaglandins in this context.

Ms. B. Malique Jones presented her work demonstrating how the urothelium drives changes to contractility that mimic neurogenic inflammatory signaling. The proposed neurogenic bladder focuses on problems with nerve coordination to promote dysregulation of continence and voiding. She is characterizing the role of the urothelium as a signaling hub. Her overarching hypothesis is that neuroinflammation increases detrusor contractility independent of its effects on afferent and efferent nerve signaling. Ms. Jones is interested in how compound 48/80 affects bladder smooth muscle contractility. She found that the compound affects efferent output, urothelium release, and purinergic and cyclooxygenase signaling, leading to increased contractility. Future studies will examine the release of the substances via the urothelium.

Dr. Ramy Goueli presented on the use of artificial intelligence (AI) in functional urology. He explained that AI has been used in studies of urolithiasis, renal cell carcinoma, urothelial cancer, and prostate cancer. Dr. Goueli explained that studies on using AI in cystoscopy have been limited. The objective of this study was to develop a machine learning algorithm to grade the severity of bladder trabeculations on cystoscopic imaging and to develop a predictive model for bladder function. The model was applied for grading trabeculations in the bladder. Future directions include correlating results to clinical measures of bladder function and developing a new model to predict invasive and noninvasive urodynamic findings and stratify patient outcomes.

Dr. LaTasha Crawford spoke on nerve injury and insights into urologic pain syndromes, with a focus on the role of sensory ganglia as a site for somatovisceral research. She is interested in studying mechanisms of communication among sensory neurons to understand chronic urologic pain and comorbid referred pain, as well as urinary dysfunction. She found that static mechanical allodynia is limited to the sural dermatome for mice following intravascular acrolein and that it persists for at least 8 days. Drawing on these findings, she hypothesized that cross-talk between injured, sensitized bladder afferents and uninjured somatosensory afferents occurs at the level of the sensory ganglia. She is investigating this topic via neurophysiology assays, calcium imaging, whole-mount staining, and genetic approaches.

Dr. Kimberly Keil Stietz spoke on the effect of developmental exposure to polychlorinated biphenyls (PCBs) on the lower urinary tract. Several mechanisms of PCB-induced neurotoxicity have been described. She is studying these effects in a mouse model and observed that PCBs enhance bladder contractility in a dose- and sex-dependent manner. The mechanisms driving these phenotypes require further investigation. Bladder inflammation might underlie changes in nerve density and voiding physiology. Contributing components of the central nervous system also must be considered.

Dr. Alison Huang presented the rationale, design, and preliminary findings from a multi-center randomized trial of a group-based therapeutic yoga program for urinary incontinence in ambulatory midlife and older women. Epidemiologic associations have been noted between physical and autonomic function and urinary incontinence in older women. Yoga has the potential to improve incontinence-related functioning and overall quality of life, but these effects had not been evaluated scientifically. Dr. Huang evaluated the outcomes of a therapeutic yoga program on incontinence. Her results indicate that pelvic yoga could result in greater reduction in total and urgency incontinence. Next steps involve examining mediators of intervention effects, exploring across subgroups, and monitoring persistence of improvements.

### Scientific Session 5: Ureters and Urolithiasis

Moderators: Kristina Penniston, Ph.D., UW–Madison (U24)

Brent Cao, University of Illinois; Children’s Hospital of Philadelphia (CHOP)–University of Pennsylvania (P20)

Speakers: Yuemeng Li, CHOP–University of Pennsylvania (P20)

*Abhay Singh, Drexel University, CHOP–University of Pennsylvania (P20)*

*John Dolbow, Ph.D., Duke University (P20)*

*Michael Lipkin, M.D., Duke University (P20)*

*Sonia Fargue, Ph.D., The University of Alabama at Birmingham (P20)*

Ms. Yuemeng Li discussed segmentation and registration of kidney stones on computed tomography (CT) imaging. Her goal is to create an automated tool to accurately identify and measure kidney stones on CT scans. This involves developing image segmentation and image registration techniques. Using urogram scans, she developed a deep learning model for urinary tract segmentations. The algorithm detected individual kidney stones with 100 percent sensitivity. She is using the model to determine how kidney stones distribute spatially within the kidney and across subjects.

Mr. Abhay Singh spoke on the use of machine learning to predict spontaneous ureteral stone passage, which could enable better individualized care. Using clinical data, he is creating computational models that use various factors from patient clinical and imaging data to predict spontaneous ureteral stone passage. Mr. Singh used an orthogonal measurement product—which multiplied the axial horizontal and vertical distances for relevant variables—to improve the models. The model could be used to promote shared decision-making between patients and their physicians when determining treatment options for ureteral stones. Mr. Singh plans to refine and integrate these models in the future.

Dr. John Dolbow presented his research on developing model-based simulations of laser ablation. The models are focused on capturing the most important components, such as the laser–fluid, fluid–stone, and laser–stone interactions, as well as damage that gives rise to surface removal. He is interested in understanding the relative importance of photothermal ablation versus fluid loadings. A thermal model was developed and calibrated against experimental data by adjusting the effective laser energy at the ablated surface. Both the model and simple theoretical analysis indicate that only a small portion of the incoming laser energy is required to explain the resulting crater volumes.

Dr. Michael Lipkin discussed optimization of settings for thulium fiber laser lithotripsy compared to settings used for holmium lithotripsy. Specific considerations include heat generation, as well as energy and frequency combinations. Dr. Lipkin found that cavitation appears to play a minimal role with thulium lasers, despite its importance for other techniques. Further studies are needed to determine ideal conditions and settings for dusting, and the effects of stone composition when using thulium lithotripsy should be explored.

Dr. Sonia Fargue spoke on endogenous oxalate synthesis in calcium oxalate stone formers. Her research is focused on addressing increases in synthesis, influences of body mass index (BMI), and other factors that affect net gut absorption of oxalate. She found that differences in dietary oxalate intake cannot fully explain the greater urinary oxalate excretion in kidney stone formation. Increased oxalate synthesis appears to be associated with stone formation. Urinary oxalate secretion was associated with BMI, possibly as a function of muscle mass. Future studies will focus on exploring changes in endogenous oxalate synthesis, as well as factors that affect net gut absorption of oxalate.

## Poster Sessions

CAIRIBU-affiliated trainees and early stage investigators were invited to submit abstracts for presentation as posters at the annual meeting. A total of 45 posters were presented in three sessions during the meeting. Drs. Macoska and Strand led the 2022 Abstract and Poster Session Committee. The following presenters were selected as the winners of the poster competition:

* Seth Reasoner, Vanderbilt University

*Defining the Infant Urobiome*

* Alejandro Roldán-Alzate, Ph.D., UW–Wisconsin

*Investigation of Lower Urinary Tract Biomechanics Using Dynamic MRI and Computational Fluid Dynamics*

* Michael Odom, Ph.D., Duke University

*Detrusor Contractility via FP Receptor Activation Is Increased in Diabetic Mice With Bladder Underactivity*

* Nicholas Steers, Ph.D., Columbia University

*Defining the Bladder Resident Macrophage Populations in the Steady State and in Response to an Immunological Challenge*

* Michael Neugent, Ph.D., The University of Texas at Dallas

*The Taxonomic Ecology and Functional Potential of the Urobiome Is Shaped by Recurrent Urinary Tract Infection and Estrogen in Postmenopausal Women*

## Key Themes

### Investigating the Basis of Individual- and Population-level Variation

Benign GU conditions reflect numerous individual lifestyle and environmental factors and often are observed in association with comorbid conditions, such as atherosclerosis, diabetes, and metabolic syndrome. Many of these conditions also are associated with aging, but the interplay among these lifestyle and environmental factors is not fully understood. These individual distinctions must be addressed during diagnosis and treatment using a personalized approach.

For example, obesity influences the development of many GU-related symptoms, as well as responses to treatment, but numerous contributing factors of obesity (e.g., BMI, fat distribution, history of obesity, inflammation, diet, physical activity) must be considered. Other lifestyle aspects to consider include alcohol intake and smoking. These complex elements represent new opportunities for investigations in research, as well as interventions in clinical practice.

Race, ethnicity, and sociodemographic disparities contribute significantly to disease susceptibility. Researchers must record and account for biological differences associated with race and ethnicity (e.g., differences in the urinary microbiome), but these dynamics have not been characterized fully and need to be better understood. Sex as a biological variable also must be considered, and the underlying causes of sex differences in GU research (e.g., urinary microbiome composition, bladder mechanical properties) have not been explored fully.

### Developing Models for Disease

Many researchers use animal, tissue, cellular, and computational models to mimic the characteristics of benign GU physiology and dysfunction in humans. During the meeting, speakers expressed the need for further development of relevant models for disease. One speaker reminded participants of the words of Dr. George E. P. Box, a British statistician who stated that “all models are wrong, but some are useful.” Speakers highlighted various ways in which they have applied models as useful tools for their research. Animal models—primarily mice—were used in studies of inflammation, macrophage populations, UPEC infection and cellular response, bladder filling, receptor activation, the aging bladder, sensory outflow, sensory ganglia, and toxin exposure. Additionally, computational models were developed for studies of bladder wall stretch and stress, bladder function, the presence of kidney stones, spontaneous ureteral stone passage, and laser ablation.

### Harnessing New Technologies and Resources for Benign GU Research

In recent years, many new technologies have become common in clinical practice. For example, quantitative imaging approaches provide new capabilities for diagnosis in various organ systems. Historically, however, imaging has played a limited role in assessing BPH/LUTS. New imaging approaches also can help improve diagnosis; qualitative approaches are deficient for detecting disease. Furthermore, genomic sequencing has become a common approach in studies of various congenital disorders—as the costs associated with genomic technologies have decreased in recent years—yet genomic studies in the context of benign GU conditions remain relatively unexplored. New laser technologies provide novel capabilities for treating kidney stones, but a better understanding of the mechanism of these approaches is needed. Applications of AI within the benign GU field also were discussed.

Several speakers highlighted public data resources and biobanks—such as the [Human BioMolecular Atlas Program (HuBMAP)](https://hubmapconsortium.org/), [Human Cell Atlas](https://www.humancellatlas.org/), [Ontology Lookup Service](https://www.ebi.ac.uk/ols/index), [*All of Us* Research Program](https://allofus.nih.gov/), and [Electronic Medical Records and Genomics (eMERGE) Network](https://www.genome.gov/Funded-Programs-Projects/Electronic-Medical-Records-and-Genomics-Network-eMERGE)—which can serve as valuable tools for benign GU research. Additionally, speakers also highlighted the [NIDDK Information Network (dkNET)](https://dknet.org/), a search portal that helps researchers access reagents, organisms, software tools, databases, and services relevant to their research.

### Building Translational Teams Through Interdisciplinary Collaboration

CAIRIBU provides a platform for partnership among clinicians and researchers from numerous disciplines. Engagement of multiple interdisciplinary specialists is critical for addressing the complexity of benign GU conditions. For example, research on other organs and organ systems (e.g., liver, kidney, gastrointestinal tract, nervous system) can provide insight into the dynamics of the GU system. These collaborations require investment of time and money but have the potential to expand access to new funding and research resources.

The CAIRIBU Interactions Core conducts a progress survey to better understand the impact of CAIRIBU efforts on cross-institutional research, collaborative proposals, and funding. The overall goal is to use these data to improve efforts to enhance and foster interactions among Centers and Programs. Opportunities for further interactions through CAIRIBU include Center symposia, graduate student seminars, K12 Scholar seminars, Advancing the Research Capacity of Trainees and Investigators at early-Career Stages (ARCTICS) community forums, CAIRIBU catalyst conversations, CAIRIBU connections, CAIRIBU urinary microbiota research interest group, social media channels, CAIRIBU workshops on collaborative research, and CAIRIBU community and stakeholder engagement events.

## NIDDK Program Officers

* Julie Barthold, M.D., Project Scientist, Division of Kidney, Urologic, and Hematologic Diseases (KUH)
* Deepak Nihalani, Ph.D., Program Official, KUH
* Chris Mullins, Ph.D., Program Consultant, KUH

## Urology Centers Program Interactions Core Staff

* Kristina Penniston, Ph.D., Director, Principal Investigator, UW–Madison
* Betsy Rolland, Ph.D., M.L.I.S., M.P.H., Co-Investigator, UW–Madison
* Jennifer Allmaras, M.P.H., Research Program Coordinator, UW–Madison
* Mariana Coughlin, M.S., Administrative and Social Media Coordinator, UW–Madison

## Consortium Monitoring Board for CAIRIBU O’Brien Urology Centers and CAIRIBU Interactions Core

* Mark Nelson, Ph.D., The University of Vermont (Chair)
* Cecilia Lo, Ph.D., University of Pittsburgh
* Shuk‑Mei Ho, Ph.D., University of Arkansas for Medical Sciences
* Dean Assimos, M.D., The University of Alabama at Birmingham