National Institutes of Health
National Institute of Diabetes and Digestive and Kidney Diseases

Annual Meeting
Collaborating for the Advancement of Interdisciplinary Research in Benign Urology

Virtual Meeting
December 2–3, 2021

DRAFT EXECUTIVE SUMMARY

Overview of the Meeting

The purpose of the Collaborating for the Advancement of Interdisciplinary Research in Benign Urology (CAIRIBU) annual meeting is to bring together the Directors of the National Institute of Diabetes and Digestive and Kidney Diseases U54 O'Brien Urology Centers and their research teams, the Directors and research teams of the P20 Exploratory Centers for Interdisciplinary Research in Benign Urology, and the Directors of the Multidisciplinary K12 Urologic Research (KURe) and Urological Epidemiology (KEpi) Institutional Research Career Development Programs and their scholars. Collectively, these Centers and Programs are part of the CAIRIBU umbrella. The CAIRIBU 2021 meeting promoted interactions among Centers and Programs and among CAIRIBU investigators and the broader benign urologic research community. Primary objectives included sharing research resources and advancing students and early-stage investigators in their development as future leaders in the field of benign urology.

CAIRIBU aims to address challenges facing researchers interested in benign genitourinary (GU) conditions, which are relevant to multiple medical specialties. Benign GU conditions have become normalized and accepted among clinicians because they often are regarded as quality-of-life conditions. Many benign GU conditions are not screened routinely and thus become apparent only when symptoms are recognized and reported. Additionally, objective markers are lacking. GU conditions often are treated by surgeons who have limited time to think like scientists. Stigma surrounding GU conditions has limited self-reporting, advocacy, funding, and—consequently—the usefulness of big data for analysis. Furthermore, the benign GU workforce pipeline is insufficient to meet current needs for diversity and breadth of study. CAIRIBU provides a platform for knowledge transfer and uptake, facilitates awareness of the breadth of benign GU research, emphasizes intersections and shared objectives, encourages networking and collaboration, and creates a sense of community. During this year's meeting, each CAIRIBU Center was represented on the agenda. A total of 231 preregistered attendees represented 70 different organizations, of which 58 percent were from the CAIRIBU community. The meeting agenda included five scientific sessions, two keynote lectures, five poster sessions, and three concurrent interactions sessions.

Scientific Sessions

Scientific Session 1: Knowledge Gaps in Benign Genitourinary Research

Moderators: *Lauren Baker, D.V.M., Ph.D., University of Wisconsin–Madison (KURe)*
Giulia Lane, M.D., M.S., University of Michigan (KUroEpi)

Speakers: *Alison Huang, M.D., University of California, San Francisco–Kaiser Permanente (KUroEpi)*
Jonathon Schmitz, M.D., Ph.D., Vanderbilt University (P20)
Jill Macoska, Ph.D., University of Wisconsin–Madison (U54), University of Massachusetts Boston
Don DeFranco, Ph.D., University of Pittsburgh (U54)
Wenkuan Xin, Ph.D., The University of Tennessee Health Sciences Center (P20)
John Knight, Ph.D., The University of Alabama at Birmingham (P20)
Ali Gharavi, M.D., Columbia University (U54)

Dr. Alison Huang described knowledge gaps related to the burden of disease. Dr. Huang identified areas requiring further study: the impact of urinary incontinence (UI) on functioning and well-being in older women from racial or ethnic minority groups, the burden of GU conditions on the broader social ecology, how GU conditions exacerbate and arise from other overlapping conditions, and side effects and the benefit-to-risk ratio of treatments for GU conditions across specific populations.

Dr. Jonathon Schmitz highlighted the need for integration across disciplines in the areas of clinical microbiology and urology. He explained that laboratory and clinical researchers have different fundamental missions, and both perspectives should be considered in the context of benign GU conditions. Clinical-use metagenomics could be used for urobiome profiling. Dr. Schmitz also proposed that clinical microbiology can help drive research; he noted that its strengths include the sheer number and diversity of wild-type specimens, linkage to electronic health records (EHRs) and data on patients, and moving beyond simplified experimental models of pathogenesis and host interaction.

Dr. Jill Macoska presented on gaps related to health disparities in benign GU conditions. She explained that more studies are needed to identify genetic determinants of health across different racial or ethnic communities. Additional resources in this area that are needed include annotation of ethnic origin in human data, inclusion of ethnic diversity in studies involving human subjects, funding opportunities for benign urologic health disparities research, and assistance with access to inclusive biorepositories and databases.

Dr. Don DeFranco detailed knowledge gaps related to mitochondrial and GU dysfunction (e.g., lower urinary tract symptoms [LUTS]), particularly with aging. Dr. DeFranco proposed that studies of pulmonary fibrosis and mitochondrial dysfunction can provide pathological insights. He identified two challenges: (1) understanding why mitochondrial dysfunction associated with LUTS in aging males is not confined to the prostate and (2) identifying metabolic adaptations to specific mitochondrial dysfunction that are compromised in the lower urinary tract of aging males.

Dr. Wenkuan Xin spoke on the need to better understand the roles of G protein–coupled receptors (e.g., bitter taste receptors) in underactive bladder. Dr. Xin identified two aims: (1) determine gene and protein expression profiles of the receptors and coupled G proteins in bladder smooth muscle and the spatial correlation between gustducin and phosphodiesterases and (2) elucidate receptor-mediated regulation of bladder smooth-muscle contractility and investigate the underlying signaling mechanisms.

Dr. John Knight highlighted unknowns and future research directions related to sources of urinary oxalate. Dr. Knight explained that knowledge gaps in this area include (1) factors influencing oxalate synthesis and (2) whether oxalate synthesis differs in calcium oxalate kidney stone formers. He noted also that future collaborative research includes low-oxalate diets to examine endogenous oxalate synthesis and controlled diets varying in oxalate to define dietary oxalate handling in enteric hyperoxaluria and microbial gut oxalate degradation.

Dr. Ali Gharavi discussed opportunities for application of genomic medicine in benign urology. He emphasized that the combination of common and rare genetic variations in adult-onset benign urologic disorders has not been explored fully. Biobanks and EHRs can be used to analyze a wide variety of traits, allowing researchers to conduct multiple analyses in parallel. The integration of omics data can further delineate disease pathways and point to potential therapies, and collaborations with benign urology networks would enable further discovery.

Scientific Session 2: Resources for Benign Genitourinary Research

Moderators: *Alexis Adrian, University of Wisconsin–Madison (U54)*
LaTasha Crawford, V.M.D., Ph.D., University of Wisconsin–Madison (KURe)

Speakers: *Anne-Catrin Uhlemann, M.D., Ph.D., Columbia University (U54)*
Douglas Strand, Ph.D., University of Wisconsin–Madison (U54), The University of Texas Southwestern Medical Center
Renee Vickman, Ph.D., NorthShore University HealthSystem (P20)
Emily Davidson, M.D., Medical College of Wisconsin (P20)
Kyle Wood, M.D., The University of Alabama at Birmingham (P20)
Kevin Wang, Ph.D., Duke University (P20), Virginia Polytechnic Institute and State University
Justin Ziemba, M.D., M.S.Ed., Children's Hospital of Philadelphia–University of Pennsylvania (P20)

Dr. Anne-Catrin Uhlemann presented on microbial genomics resources to support urinary tract infection (UTI) research. She explained that virulence factors are encoded on the variable core chromosome, and antimicrobial resistance genes are plasmid-encoded. The Columbia University U54 Center is pursuing two new approaches—full-length 16S rRNA sequencing and nanopore sequencing—to better characterize microbial genomes. The Center also maintains a biosample repository of samples from patients with UTI.

Dr. Douglas Strand highlighted human tissue and data resources for benign urology. The GenitoUrinary Development Molecular Anatomy Project (GUDMAP) Consortium contains a collection of novel epithelia in human prostatic urethra. Dr. Strand's laboratory maintains a biorepository with clinically annotated specimens from donors. Researchers also can review data sets associated with publications, as well as the biorepository, through Dr. Strand's laboratory website.

Dr. Renee Vickman described her work on *in vivo* modeling of tumor necrosis factor alpha–antagonist therapy for suppressing benign prostatic hyperplasia (BPH). The treatment of autoimmune disease appears to have an effect on BPH pathology. Dr. Vickman's team studied this relationship in mouse models and human patients. She emphasized that the P20 resource played a crucial role in isolation of leukocytes from small and large male BPH tissues. A prostate tissue biorepository provides access to full clinical annotation.

Dr. Emily Davidson presented on integration of EHR-based tools for diagnosis and treatment of women's UI. The Translational Interdisciplinary Genito-Urinary Research (TIGUR) program has two specific aims: (1) routinely measure patient-reported UI in a racially diverse population of adult women in primary care

and (2) pilot test a guideline-based UI care pathway that integrates primary and specialty care. Resources for patients include informational videos, the Tät App, and referral to the Mind Over Matter program.

Dr. Kyle Wood outlined resources available at The University of Alabama at Birmingham to answer questions related to the endogenous oxalate pathway. These resources are available through the institution's transgenic and genetically engineered models core, small-animal microsurgical core, microbiome core, metabolism core, mass spectrometry/proteomics shared facility, and Civitan International Neuroimaging Laboratory. Collaborations (e.g., academic, industry) and mentorship also provide key resources.

Dr. Kevin Wang detailed efforts to develop a physics-based computational model of laser–fluid–solid interactions to characterize the effects of shockwave and laser lithotripsy therapies. Computational challenges include implicit interface tracking methods, prediction of stone fracture of shockwave therapy, optimization of shockwave profile for maximum stone damage, simulation of cavitation bubble dynamics, and prediction of laser-induced cavitation and its effects. Dr. Wang explained that the model is being developed presently, and all codes are open source.

Dr. Justin Ziemba described how machine learning (ML) can improve diagnosis and treatment. He presented a hypothetical case of a woman with kidney stones, outlining the steps of initial presentation, initial differential diagnosis, diagnostic imaging, treatment planning, and treatment outcomes. Dr. Ziemba explained how recommendations for patients could be personalized through interpretation of robust demographic, clinical, and radiographic information.

Scientific Session 3: K12 Scholar "Flash Talks"—Current and Prior K12 Scholars Present Their Research

Moderator: *Jim Hokanson, Ph.D., Medical College of Wisconsin (P20)*

Speakers:
Scott Bauer, M.D., M.S., University of California, San Francisco–Kaiser Permanente (KUroEpi)
Tanya Sysoeva, Ph.D., Duke University (KURe), The University of Alabama in Huntsville
David Bayne, M.D., M.P.H., University of California, San Francisco–Kaiser Permanente (KUroEpi)
Joshias Maru, University of California, San Francisco–Kaiser Permanente (KUroEpi)
Casey Steadman, Ph.D., Duke University (KURe)
Heidi Wendell Brown, M.D., M.A.S., University of Wisconsin–Madison (KURe)
Eva Raphael, M.D., M.P.H., University of California, San Francisco–Kaiser Permanente (KUroEpi)
LaTasha Crawford, V.M.D., Ph.D., University of Wisconsin–Madison (KURe)
Petra Popovics, Ph.D., University of Wisconsin–Madison (KURe)
Matthew Grimes, M.D., University of Wisconsin–Madison (KURe)
Teresa Liu, Ph.D., University of Wisconsin–Madison (KURe)
Maryellen Kelly, D.N.P., M.H.Sc., Duke University (KURe)
Giulia I. Lane, M.D., M.S., University of Michigan (KUroEpi)

Dr. Scott Bauer highlighted his research mission to help treat older adults with LUTS by studying how aging contributes to these common benign urologic symptoms. He is developing an alternative aging framework that uses biological, phenotypic, and functional aging to understand age-related LUTS.

Dr. Tanya Sysoeva discussed her efforts to study UTIs in the context of the urinary microbiome. She is working to characterize the collection of urinary lactobacilli in samples with or without UTI. She explained that the microbiome involves a rich set of interactions, and more studies in this area are needed.

Dr. David Bayne and Mr. Joshias Maru outlined their work on underinsurance and its association with increased risk of multiple kidney stone procedures. They hypothesized that patients with limited insurance have less access to health care services, resulting in increased stone burden and worse outcomes. They completed a review of prospectively collected data, noting differences among socioeconomic and ethnic groups.

Dr. Casey Steadman detailed her research using vagus nerve stimulation to ameliorate bladder and bowel dysfunction after spinal cord injury (SCI). She hypothesized that activation of the vagal anti-inflammatory pathways will attenuate bladder and bowel remodeling and inflammation, thereby ameliorating bladder and bowel dysfunction after SCI. She is examining cell population differences and functional outcomes measures between groups in a mouse model.

Dr. Heidi Wendell Brown highlighted her efforts to assess the feasibility of the Mind Over Matter program. The program is implemented by community members, rather than health care professionals, and is disseminated through existing infrastructure. Her project involved adaptation and pilot-testing, a randomized controlled trial, implementation, and dissemination. Additionally, she discussed efforts to develop an online program with tailored engagement.

Dr. Eva Raphael presented on her work using molecular microbiology, social, and spatial epidemiology methods to identify risk factors. She hypothesized that community-onset bacteriuria caused by extended spectrum beta-lactamase (EBSL) *Escherichia coli* can occur as outbreaks and therefore should cluster by time and space. Her findings suggest a local common source exposure to specific *E. coli* genotypes but not EBSL *E coli*, which could arise from multiple point sources.

Dr. LaTasha Crawford presented her research on somato-visceral crosstalk as a neural mechanism of bladder disease. She hypothesized that sensory neurons of the bladder can communicate with sensory neurons from the skin, and injury to one set of sensory neurons can cause hyperactivity of bystander sensory neurons. She performed *ex vivo* studies to target dorsal root ganglia in neurophysiology assays, combined with molecular studies. She also is studying cell-specific mechanisms and mechanoreceptor subtypes using genetic strategies.

Dr. Petra Popovics discussed her work on prostatic inflammation and physiological changes that lead to LUTS. Her work suggests that osteopontin relates to BPH and inflammation. Osteopontin deficiency also alters the prostatic immune environment. Dr. Popovics also is studying how steroid hormone imbalance leads to inflammation.

Dr. Matthew Grimes presented his work on fibrosis in lichen sclerosus (LS) urethral stricture disease. His goal was to improve patient-centered outcomes in LS-related urethral stricture by augmenting the success of minimally invasive treatment. He found that that collagen structure is increased and altered in LS, and CD44 expression is reduced. His next steps are to (1) test the effect of reduced CD44 expression and test antifibrotic treatment and (2) examine alterations in collagen content and develop a noninvasive imaging modality.

Dr. Teresa Liu detailed her efforts to develop approaches to delay the upstream effects of aging. Mitochondrial dysfunction contributes to fibrosis-mediated BPH/LUTS. Furthermore, cellular senescence is increased in BPH nodules, and epigenetic modifications alter steroidogenesis in the prostate with age. A better understanding of these processes would lead to identification of biomarkers for the disease in blood or urine samples.

Dr. Maryellen Kelly outlined her evaluation of posterior tibial nerve stimulation to treat overactive bladder (OAB) in children. Her research objective was to determine the safety of the Urgent® PC system

in children with OAB. She is studying this treatment in a single-arm cohort study through the Pediatric Trials Network across the United States.

Dr. Giulia I. Lane detailed her efforts to explore treatment decisions and outcomes for a tailored approach to advanced OAB care. She discussed the concept of decision-making, which weighs the best available medical evidence with patients' preferences and values. In an exploratory sequential mixed methods study, she is assessing how to bring personalized care and better treatment efficacy to OAB care.

Scientific Session 4: Therapeutic Advances in Benign Genitourinary Research

Moderators: *Connor Beebout, Vanderbilt University (P20)*
Tanecia Mitchell, Ph.D., The University of Alabama at Birmingham (P20)

Speakers: *Cathy Mendelsohn, Ph.D., Columbia University (U54)*
Jonathon Barusch, M.D., Ph.D., Columbia University (U54)
Chad Vezina, Ph.D., University of Wisconsin–Madison (U54)
Naoki Yoshimura, M.D., Ph.D., University of Pittsburgh (U54)
Kelvin Davies, Ph.D., Albert Einstein College of Medicine (P20)
Indira Mysorekar, Ph.D., Washington University in St. Louis (P20), Baylor College of Medicine
Zachary Dionise, M.D., Duke University (P20)

Dr. Cathy Mendelsohn presented on repair of the urothelium. She explained that urothelial effects associated with benign diseases could contribute to patient symptoms. Her team examined whether peroxisome proliferator–activated receptor agonists could be used to repair damaged urothelium. They found that Rositra treatment restored normal urothelial differentiation. This approach could be used to repair urothelial abnormalities associated with benign disease.

Dr. Jonathon Barusch described the therapeutic potential of novel iron chelators. Using a mouse model, he is examining the early stage of damage and repair in UTI. He is assessing the expression of iron- and heme-related genes—such as *NGAL* and *HMOX*—in first 6 hours of UTI. These data can provide insight for therapeutics.

Dr. Chad Vezina outlined the development of alpha blockers and 5-alpha reductase inhibitors, integration of contemporary methods, and development of drugs to combat fibrotic disease in the urethra and prostate. He explained how integration of rodent models and urinary physiology into the research and development pipeline could improve drug development. This approach could be useful in working toward individualized therapy.

Dr. Naoki Yoshimura presented on a nerve growth factor (NGF)–targeting therapy for prostatic inflammation and LUTS. His team is examining how inflammation affects bladder function. The researchers are using rat and mouse models to study afferent sensitization following prostatic inflammation. They are using their findings to develop liposome-based therapies and tyrosine kinase receptor antagonists. NGF-targeting therapy could be effective for the treatment of storage LUTS in BPH patients with prostatic inflammation.

Dr. Kelvin Davies discussed his work on the use of nitric oxide (NO) as a treatment for erectile dysfunction (ED) associated with prostate cancer survivorship. He investigated the ability of topically applied NO-releasing nanoparticles to act synergistically with sildenafil in eliciting an erectile response in a radical prostatectomy (RP) rat model. Results suggest a novel treatment strategy for patients with ED following RP.

Dr. Indira Mysorekar discussed her efforts in developing new therapeutic regimens for the treatment of UTI. She hypothesized that in women, cystitis cystica nodules are bladder tertiary lymphoid tissue similar to those in aged mice. Her findings suggest that a multimodal prevention regimen (e.g., antibiotics, vaginal estrogen therapy, D-mannose, methenamine) is beneficial. She is working to characterize each of these components of the regimen in animal models to better understand the mechanisms of treatment and target specific events that occur.

Dr. Zachary Dionise presented on the role of cavitation and the development of a novel kidney phantom model in *in vitro* laser lithotripsy research. Dr. Dionise designed experiments to isolate the damage of cavitation bubble collapse in dusting. His findings suggest a vital role of cavitation in the process. He also is using 3-D printing technology to develop translucent, anatomically accurate *in vitro* kidney models for laser lithotripsy. Future directions involve use of the kidney model to evaluate cavitation dynamics and the evolving thulium fiber laser.

Scientific Session 5: Collaborative Research in Benign Genitourinary Research

Moderators: *Hannah Miles, University of Wisconsin–Madison (U54)*
Michael Odom, Ph.D., Duke University (KURe)

Speakers: *Kristina Penniston, Ph.D., University of Wisconsin–Madison (U24)*
Laura Pascal, Ph.D., University of Pittsburgh (U54)
Simone Sanna-Cherchi, M.D., Columbia University (P20)
Grace Morales, Vanderbilt University (P20)
Katherine Fischer, M.D., Children's Hospital of Philadelphia–University of Pennsylvania (P20)
Yuemeng Li, Children's Hospital of Philadelphia–University of Pennsylvania (P20)
Joan Neuner, M.D., M.P.H., Medical College of Wisconsin (P20)
Jonathon Pollack, M.D., Ph.D., Stanford University (U54)

Dr. Kristina Penniston presented challenges and potential within CAIRIBU. She explained that CAIRIBU'S overarching aim is to build and foster a sense of trust required to share knowledge, resources, and ideas. Challenges related to collaborative research include concern about engaging with investigators on scientific review committees, the greater magnitude of effort needed, and need for further support from the Interactions Core. Future directions include the CAIRIBU Evaluation Program and enhancement of activity and visibility within the broader benign GU research community.

Dr. Laura Pascal described how CAIRIBU has enhanced efforts to create a mouse model for BPH and LUTS through idea development, experienced advice and insights, resources, and related studies. She emphasized that CAIRIBU has fostered conversation relating to model development; future directions include using the mouse model to target prostate inflammation and determine how the mechanisms of aging in the prostate and bladder affect BPH/LUTS.

Dr. Simone Sanna-Cherchi presented on a collaborative network for studying the genetics of congenital anomalies of kidney and urinary tract (CAKUT). He explained that challenges in researching CAKUT include high genetic heterogeneity and complex architecture, the large number of candidate genes and variants, a need for mechanistic studies, and returning to human genetic and epigenetic context. The network leverages the expertise of investigators from many different areas.

Ms. Grace Morales described a collaboratively developed pipeline for analysis of microbial genomes. She explained that the microVU repository provides the basis for a computational pipeline to connect deidentified patient data with bacterial isolates. This area requires engagement among researchers, clinical microbiologists, and physicians. Future applications include leveraging genomic information, utilizing

clinical microbiology resources, pursuing translational discovery, and performing high-throughput research in uropathogens.

Dr. Katherine Fischer and Ms. Yuemeng Li outlined a collaborative approach to building an ML model for clinical urology. They explained that collaboration between urologists and ML scientists is critical to predict stone passage; constant communication between these groups is needed. Team members include medical students; urology residents, fellows, and attending physicians; bioengineering and ML faculty and doctoral students; data scientists; and research assistants. They outlined processes for study design, data collection, and model creation and discussed current efforts to develop an efficient and accurate model to predict urinary tract and urinary stone passages.

Dr. Joan Neuner highlighted collaborative efforts among primary care, subspecialty, and informatics researchers to develop a women's UI registry. Specific aims are to (1) examine the feasibility of routine measurement of patient-reported UI in a primary care–based population and (2) utilize this measure and other elements from a health system's clinical data warehouse to establish a registry to study UI health care utilization. The team is working toward implementing a learning health systems priorities approach, and the team members will use feasibility and generalizability measures to assess the registry's value for future research.

Dr. Jonathon Pollack provided an update on the Stanford O'Brien Center. He explained that the Center is focused on applying genomics technologies to study BPH. The team is developing a BPH atlas to enable a multiscale view of tissues, cells, and molecules. The Center's biospecimen/bioimaging core is essential for spatial transcriptomics and multiplex immunohistochemistry. Future directions include investigations of BPH and LUTS, utilization of Center resources, and implementation of training opportunities.

Key Themes

Overcoming the Stigma of Disease

Benign GU conditions are highly prevalent in the U.S. population and impart significant health and economic burdens at multiple levels (e.g., individual, interpersonal, organizational/institutional, community, societal, ecosystem). Affected individuals experience direct and indirect economic burdens from treatments, visits, hospitalizations, and work productivity. UI, for example, is a common reason for admission to nursing homes and can lead to depression and social isolation. Additionally, prostate cancer survivorship carries an increased risk of LUTS, including ED.

Research Gaps and Opportunities: Research gaps in primary care for benign GU conditions (e.g., UI) include the need to sponsor longitudinal studies of treatment patterns, barriers, and outcomes. Many patients fail to seek care for benign GU conditions. Factors for treatment include patient understanding, awareness of treatment options, desire for treatment, care-seeking (i.e., initial appointment), accessibility of treatment and referral, secondary appointment availability, and escalation of interventions. Presenters discussed approaches for promoting care-seeking in patients with benign GU conditions. They proposed improving access to informational resources (e.g., videos, Tät App, Mind Over Matter). Tailored online platforms are likely to be effective for patients who are uncomfortable participating in in-person treatment programs. In some instances, a shared decision-making approach—which balances the best available medical evidence with patients' preferences and values—can be beneficial.

Addressing Health and Genetic Disparities

Social and genetic determinants of health arise from various general socioeconomic, cultural, genetic, and environmental factors. Health inequities often are linked to socioeconomic status, but race and other social categories (e.g., sexual and gender minority groups) are major drivers. Many of these factors have

not been addressed fully in studies of benign GU conditions. Several presenters emphasized the complexity of this topic. For example, social and environmental pathways (e.g., personal, structural) lead to inequity and are likely to influence the prevalence of GU conditions.

The effects of benign GU conditions in underrepresented racial and ethnic populations require further exploration. Several presenters highlighted that minority racial and ethnic groups often are underrepresented in study cohorts. Furthermore, selected participants from these communities often are English-speaking and might not be representative of others from same group. Self-reporting measures—which often are used to identify benign GU conditions—might not be relevant to non-white populations. Genetic disparities also are likely to exacerbate health inequity. Non-white patients often possess more rare genetic variants, many of which are not found in databases. Additionally, tools often are developed in white populations and do not work as well in non-white populations. As a result, analysis, discovery, and diagnosis of benign GU conditions are more challenging in non-white patients.

Research Gaps and Opportunities: Current gaps in this area include annotation of ethnic origin in human data, inclusion of ethnic diversity in studies involving human subjects, improved classifications of gene variants in cohorts, funding opportunities for benign urologic health disparities research, and assistance with access to inclusive biorepositories and databases. In discussion, presenters emphasized the need to partner with individuals who have expertise in studying health disparities (e.g., designing surveys, approaching groups, engaging the community). They acknowledged that education, understanding, and outreach are crucial. Presenters also emphasized the importance of fostering diversity and inclusivity within the scientific workforce.

Fostering Integration Across Disciplines

Benign GU research spans multiple disciplines and requires leveraging numerous areas of expertise (e.g., basic and translational researchers, clinicians, bioengineers, data scientists). Comprehensive data from interdisciplinary studies are crucial in developing a full understanding of benign GU conditions.

Research Gaps and Opportunities: Presenters discussed the need to better understand overlapping conditions and physiological systems. For example, inflammation is associated with benign GU conditions, but the process is not understood fully; better characterization of the effects of the immune, nervous, and endocrine systems in benign GU conditions could provide further physiological insights. The urinary microbiome also can lead to diversity in urinary conditions; thus, clinical microbiological context also is critical to better understanding the pathogenesis of UTIs and other benign GU conditions.

Biology of Aging

Benign GU conditions are highly prevalent among older adults, but urogenital changes with age are poorly correlated with symptoms, and the pathophysiology of GU conditions remains poorly understood.

Research Gaps and Opportunities: Presenters emphasized the need to better understand the relationship between aging and GU function. Age-related mitochondrial dysfunction, for example, contributes to various aspects of cellular, organ, and tissue dysfunction that are likely to contribute to benign GU pathology in stromal and/or epithelial cells. They noted the need to consider biological, phenotypic, and functional aging. A better understanding of aging-related processes could lead to identification of biomarkers for GU conditions and, ultimately, treatments to target the underlying hallmarks of disease.

Individualized Medicine

A better understanding of disease could provide increased opportunities for individualized medicine—therapeutic approaches that are tailored to each patient's susceptibility and response to disease.

Research Gaps and Opportunities: Individuals respond differently to treatments for benign GU conditions (e.g., BPH), and physicians typically begin with one treatment and continue until an effective treatment is found. This approach often leads to overtreatment. Presenters discussed the application of targeted therapy, biomarkers, molecular phenotyping, and multi-omics integration for development in this area. ML also can be used to personalize diagnosis and treatment pipelines through the use of robust demographic, clinical, and radiographic information to improve treatment outcomes.

Development of Animal Models

Presenters offered different perspectives on the use of animal models in benign GU research. Several presenters highlighted the difference in urological anatomy between rodents and humans, which creates challenges in the development of mouse or rat models for various benign GU conditions. Others, however, presented evidence highlighting the use of mouse and rat models to understand the cellular anatomy and molecular physiology of disease. The development of a zebrafish model for high-throughput screening of congenital anomalies of kidney and urinary tract also was discussed. This approach allows more efficient screening of multiple genes and interactions, which is not feasible in mouse models.

Research Gaps and Opportunities: Availability of intact human tissue for translational research often is limited. For this reason, animal models can provide researchers valuable preclinical insight into human disease. Several presenters, however, noted the limitations of animal models for studying certain conditions (e.g., BPH) that are unique to humans. They emphasized the value of large human data sets for understanding the molecular basis of disease. Additionally, several presenters noted that organoids from human tissue could provide an alternative approach for researchers.

Data Resources

Advances in genomic technologies have enabled the generation of large data sets that can provide insight into the molecular basis of benign GU conditions. These data sets offer new opportunities and challenges within the field. A growing need exists to ensure that data sets are made accessible to the scientific community. Data sharing is crucial for scientific advancement and reproducibility. Increasingly, scientific journals are working to ensure that data are compliant with FAIR (Findable, Accessible, Interoperable, and Reusable) Data Principles. These principles help enable data discovery and access, data processing, data curation and publication, and data visualization. Several presenters highlighted data repositories (e.g., The Cancer Genome Atlas, GUDMAP, microVU) that are available to the research community.

Research Gaps and Opportunities: The integration of omics data can further delineate disease pathways and point to potential therapies (e.g., discovery of molecular signatures of benign urologic disease). Presenters discussed efforts in applying genomic technologies to develop molecular atlases, characterize cellular subtype populations, and perform spatial transcriptomics. Presenters also highlighted recent efforts to optimize sequencing techniques and develop computational models for analyzing large data sets.

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