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[Round Robin – Friday, July 18]

Introduction

Scott Bauer, MD, ScM

Associate Professor

- Depts of Medicine, Urology, Epidemiology & Biostatistics, University of California, San Francisco

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Research Interests & Goals

Research Focus Areas

- Geriatric urology, esp diagnosis/treatment of LUTS in older adults
- Geroscience (aging biology) mechanisms
- Clinical trials of novel targets for LUTS in older adults or accelerated aging phenotypes (e.g., obesity, HIV)

Primary Topics

- Association of LUTS with geriatric outcomes
- Modifiable risk factors for LUTS in older adults/accelerated aging
  - Physical/cognitive function, sarcopenia, frailty, adiposity
- Identifying and targeting geroscience-informed LUTS mechanisms
  - Mitochondrial function, mTOR, senescence

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Key Expertise & Methods

Core Knowledge & Expertise

- Rigorous epidemiologic methods
- Clinical implications and practice guidelines (primary care, urology, urogynecology)
- Accessing existing data or specimens

Skill Set

- Clinical epidemiology, causal inference, longitudinal models, biomarkers, clinical outcomes
- Secondary data analyses using existing data or samples, clinical trials (recently acquired skill)
- Collaborating with investigators who have novel measurements or pre-clinical models
- Grant-writing, framing research problems

Introductions to large aging-focused research networks, identifying existing human datasets, study design advice

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Ongoing/Recent Projects

SOMMA Cohort

Indefinite (leadership role)

- Prospective cohort of 1300 adults age 70-90, deep aging phenotype, serum proteomics, thigh muscle biopsy, full-body MR including pelvis, LURN SI-10
  - LUTS/bother: integrative > muscle
  - UI: muscle/power > integrative
  - Walking energetics
  - Women > men
- NIA K76 Beeson
- DeLancey (Michigan-imaging), Molina (UCSD-mito), Cawthon (UCSF-muscle)

PROUD Pilot Trial

3/2023 to 3/2026 (+NCE)

- Pilot clinical trial of remotely supervised home-based exercise intervention for LUTS/BPH in 70 sedentary older men
  - LUTS, uroflow/PVR, physical function, extensive biobank
  - PBMC/platelet respirometry
  - 70% of recruitment goal
- NIDDK R01
- McVary (Loyola- urology), Molina (UCSD-mito), ?industry (proteomics)

Your Thoughts:
Major Knowledge Gaps in the Field

Age-related LUTD =/= symptoms

- Age-related changes in LUT tissues/physiology are weakly correlated with symptoms, what are the necessary/causative factors? What are the resilience factors?
- Pre-clinical models cross-referenced with human studies -> systematic process of screening

Effects of anti-aging interventions

- Multiple interventions slow/reverse aging biology across several organs/tissues, which ones affect LUT tissues/physiology the most?
- Animal trials cross-referenced with human trials -> systematic process of screening

Non-invasive LUTD measures

- Need to large observational studies of humans without disease who are deeply phenotyped and followed for a long time → measures can't be too invasive
- Measurement development, esp stress tests that can bring out subclinical dysfunction

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Introduction

Alison Huang, MD, MAS

Professor of Medicine, Urology, & Epidemiology & Biostatistics

- University of California San Francisco
- Director, Urological Epidemiology K12 Program
- Director, Women's Health Clinical Research Center
- JAMA+ Clinical Trials Channel

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Research Interests & Expertise

Research Focus Areas

- Evaluating the efficacy, safety, and accessibility of treatment strategies for genitourinary syndromes in older adults (esp. women)
- Addressing shared factors underlying symptomatic genitourinary dysfunction and other aging/geriatric syndromes in older adults

Primary Topics

- Geriatric incontinence in older women
- Nocturia and sleep in older adults
- Genitourinary syndrome of menopause
- Chronic pelvic pain across the aging spectrum

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Key Expertise & Methods

Core Knowledge & Expertise

- Participant-oriented research on genitourinary symptoms in older women
- Generalist perspective on diagnosis and management of genitourinary conditions

Skill Set

- Randomized clinical trial design and methods
- Community-based participant recruitment and engagement
- Development and validation of patient-reported outcome measures

Resources: access to data and populations from clinical trial and epidemiologic studies of midlife and older adults with urinary symptoms

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Ongoing/Recent Projects

LILA trial

2018-2025

- Multisite RCT of a pelvic floor yoga vs. physical conditioning program for midlife and older women with stress-, urgency-, or mixed-type urinary incontinence (N=240)
- NIDDK R01/NIA K24
- Collaborators: Leslee Subak, Margaret Chesney, Wendy Mendes, Scott Bauer

TRIUMPH trial

2022-present

- Multicenter RCT comparing the cognitive and multi-system outcomes of different pharmacologic treatment strategies for urgency incontinence in older ambulatory women (N~270)
- NIA R01
- Collaborators: Kristine Yaffe, Louise Walter, Leslee Subak, Erica Kornblith, Jing Cheng, John Newman

Ongoing/Recent Projects

PLUM trial

2023-present

- Multicenter placebo-controlled RCT of letrozole (aromatase inhibitor) therapy for symptomatic uterine leiomyomata (fibroids) (N~140)
- NICHD R01
- Collaborators: Vanessa Jacoby, Kedra Wallace, John Boscardin, Ram Parvataneni, Craig Sobolewski

POPPY trial

2022-present

- Fully remote randomized trial of a pelvic yoga program for women with chronic pelvic pain syndrome recruited nationally (N~220)
- NCCIH R01
- Collaborators: Carolyn Gibson, Maria Chao, Jing Cheng, Leslee Subak, Francesca Nicosia, Tami Rowen

Your Thoughts:
Major Knowledge Gaps in the Field

Methodologic gap: Limited ability to study lower urinary tract symptoms “in the field”

- Gap: Lack of feasible methods for evaluating individual, environmental, behavioral triggers for ongoing symptoms in the usual care settings or everyday lives of older adults
- Need: Collaboration to develop and implement new tools for collecting physiologic, microbial, and other participant data that can be integrated into community-based studies

Methodologic gap: Barriers to conducting rigorous, efficient, generalizable RCTs

- Gap: Trials provide the gold standard for evidence about interventions but tend to be costly, are highly bureaucratic, and often engage overly narrow populations
- Need: Collaboration to develop more streamlined processes, standards, and pathways for trial activation and implementation across clinical, regulatory, health system partners

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Your Thoughts:
Major Knowledge Gaps in the Field

Clinical/public health gap: Evaluation and Treatment for OAB

- Gap: Limited, modestly effective, inaccessible, poorly tailored treatment (partly due to heterogeneous and multifactorial nature of the syndrome)
- Need: Collaboration to develop and test more accessible strategies to phenotype and tailored treatment for older adults in outpatient generalist care

Clinical/public health gap: Recurrent UTI management in older outpatients

- Gap: Confusion about who, when, how to test and treat older women in the community (leading to either antibiotic resistance or recurrent urosepsis)
- Need: Collaboration to develop more expansive healthcare-system embedded diagnostic and treatment research networks (for strategies arising from basic/translational research

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Introduction

Zohreh Izadifar, PhD

Research Faculty

- Boston Children's Hospital, Harvard Medical School
- Urology Department, Department of Surgery

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Research Interests & Goals

Research Focus Areas

- Bioengineering human urogenital tissues and microphysiological systems
- Preclinical in vitro disease modeling, drug discovery and screening
- Patient-derived urogenital model systems

Primary Topics

- Development and application of human in vitro models of urogenital organs
- Studying biological factors/mechanisms deriving health and diseases using physiological human in vitro models
- Preclinical testing of candidate interventions

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Key Expertise & Methods

Core Knowledge & Expertise

- Tissue engineering, primary human in vitro models, 3D biofabrication
- Modeling and studying mucosal biology, pathophysiology, host-microbiome interactions
- Multi-modal characterization techniques; cellular, molecular, and functional assays

Skill Set

- Bioengineering in vitro models, human tissue biofabrication, biosensors
- Microphysiological systems, Organ-on-Chip, Organoids, Transwell cultures
- Isolation, culture, and banking of patient-derived primary human urothelial cells, host-microbiome interaction studies, preclinical drug testing

Organ-Chip models, primary human urogenital biobank (epithelial and stromal cells, tissues, urine, medical metadate [male, female, adult, pediatric])

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Ongoing/Recent Projects

Engineering Next-Generation Human In Vitro Models for Advancing Urological Health

2024-

- Developing preclinical, human-relevant in vitro models of male and female bladder and urethra using Organ Chip technology, physiologically relevant microenvironmental cues, and patient-derived primary cells
  - Created biobank of lower UT primary cells and tissues (>25 patient)
- Startup package
- BCH (Boston), NDRI

Personalized BV Treatments: Harnessing Organ Chip Models to Tackle Health Inequity

2024-2026

- Studying donor-specific difference in cervical mucosa host immunity and responses to bacterial vaginosis pathogens and treatments using preclinical human Cervix Chip in vitro models developed using cells from women of diverse genetic backgrounds (African and Caucasian)
  - Created biobank of cervical cells and tissues (>12 donors)
- Foundation fund
- BCH, MGH (Boston), NDRI, University of Nairobi (Kenya)

Your Thoughts:
Major Knowledge Gaps in the Field

Mechanisms driving sex-specific health & chronic uro-aging and diseases

- Complex dynamic microenvironment of sex-specific urogenital mucosa, stroma, microbiome, hormones, systemic and local immunity, and cross-organs interactions are limitedly understood
- Plan multidisciplinary projects that enables bridging of mechanistic knowledge from multiple perspectives for a holistic approach to study mechanisms of urogenital diseases (i.e., uro-aging)

Lack of physiological human relevant model

- No physiological models of human urethra or female bladder, low-fidelity bladder models using immortalized male cell lines – no relevant functional and biomechanical characteristics, no age consideration
- Strategic collaborations to leverage new model systems, biospecimen/cells, and established models

Disconnected basic and clinical research

- No effective pipeline for bench-to-bedside translation
- Create collaborative teams with basic and translational expertise to walk the walk from novel discoveries in the field to preclinical validation and IND application

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Introduction

Teresa Liu, PhD

Research Assistant Professor

- University of Wisconsin - Madison
- Department of Urology

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Research Interests & Goals

Research Focus Areas

- Steroid hormone signaling changes through age
- Hallmarks of aging in the lower urinary tract
- Longevity interventions in reversing urinary dysfunction

Primary Topics

- Epigenetic regulation of steroid metabolism genes
- mTOR signaling as a master regulator of prostatic aging
- Exercise and dietary restriction to modulate voiding

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Key Expertise & Methods

Core Knowledge & Expertise

- Mouse models of aging and voiding dysfunction
- Longevity interventions (e.g., exercise, dietary restriction) in mouse models
- Prostate cell biology

Skill Set

- CRISPR/Cas9, shRNA, siRNA
- Histology, immunohistochemistry
- Genomics, transcriptomics analysis

No resources to share yet

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Ongoing/Recent Projects

Aging estrogen steroidogenesis

Ended April 2025

- Estrogen signaling is altered in LUTS/BPH
  - Epigenetic alterations mediate lowered ERβ signaling in disease
  - Increased accumulation of ERβ ligands delays onset of urinary dysfunction
- NIA K01
- Will Ricke, Don DeFranco, Laura Pascal

mTORC1 modulation in prostate

Resubmission October 2025

- mTORC1 is a master regulator of aging in the prostate
  - mTORC1 mediates mito dysfunction, senescence, and autophagy
  - Exercise and AA restriction improve urinary dysfunction
- NIDDK/NIA R01
- Laura Pascal, Don DeFranco, Dudley Lamming

Your Thoughts:
Major Knowledge Gaps in the Field

Which hallmarks of aging are most responsible for LUTS/BPH?

- What is the normal progression of aging within the prostate?
- Longitudinal assessment of mechanisms of aging within the prostate correlating to changes in symptoms.

How do longevity interventions function to alleviate LUTS/BPH?

- Several longevity interventions work in preclinical models, but more need to be tested.
- Examining LUTS in ongoing human longevity trials – synergy between aging and urology research.

Lack of multidimensional impact of the aging prostate.

- LUTS/BPH associated with other aging diseases/disorders but which factors are systemic?
- Aging occurs from the molecular level through the meta-organism. We need to examine outside the prostate as well.

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Introduction

Indira Mysorekar, PhD

Position

- Baylor College of Medicine
- Medicine/Infectious Diseases
- Huffington Center on Aging

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Research Interests & Goals

Research Focus Areas

- Urinary tract infections in menopausal women
- Bladder mucosal immunity in aging
- Urothelial cellular biology/dynamics in response to infection, aging…
- Sex differences in bladder disease susceptibility
- Development of scalable urothelial organoid models
- *Placental infections and immunity*

Primary Topics

- Uro-aging; inflammaging; urothelial cell biology

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Key Expertise & Methods

Core Knowledge & Expertise

- Mouse models of bladder disease
- Translational research in urology/urogynecology
- Infection
- Immunology

Skill Set

- Infection
- Mouse models; iPSC, tissue organoid models; humanized models; human sample/tissue biobanks; human clinical studies
- scRNA-Seq; metabolomics; proteomics; integrated multiomics; tissue histopathology

Urinalysis; histopathology; immune cellular analysis

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Ongoing/Recent Projects

Cellular and molecular mechanisms governing aging in the bladder

Project 1

- Urothelial aging; proteostasis
- NIA

- Jason Mills

Mechanisms of Age-and Sex- Dependent Changes in Urinary Bladder Immunity

Project 2

Bladder mucosal immunity in aging

- NIDDK

Your Thoughts:
Major Knowledge Gaps in the Field

[Critical Gap #1]

- Scalable tools to study mechanisms and interventions

[Critical Gap #2]

- Investment in understanding and treating LUTD in older women (and men)
- Understanding the Dynamics of the Aging Process

[Critical Gap #3]

- [Additional dUnderstanding of impact of bladder immunity and epigenetics on disease susceptibility
- etail]

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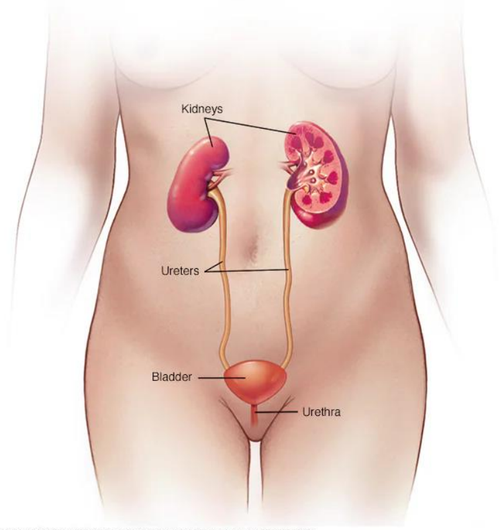
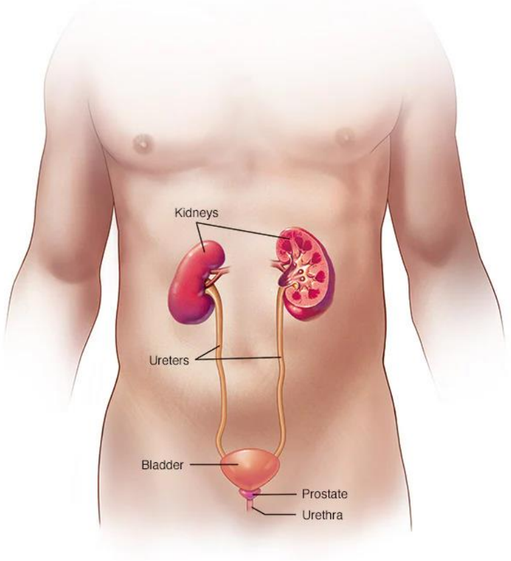
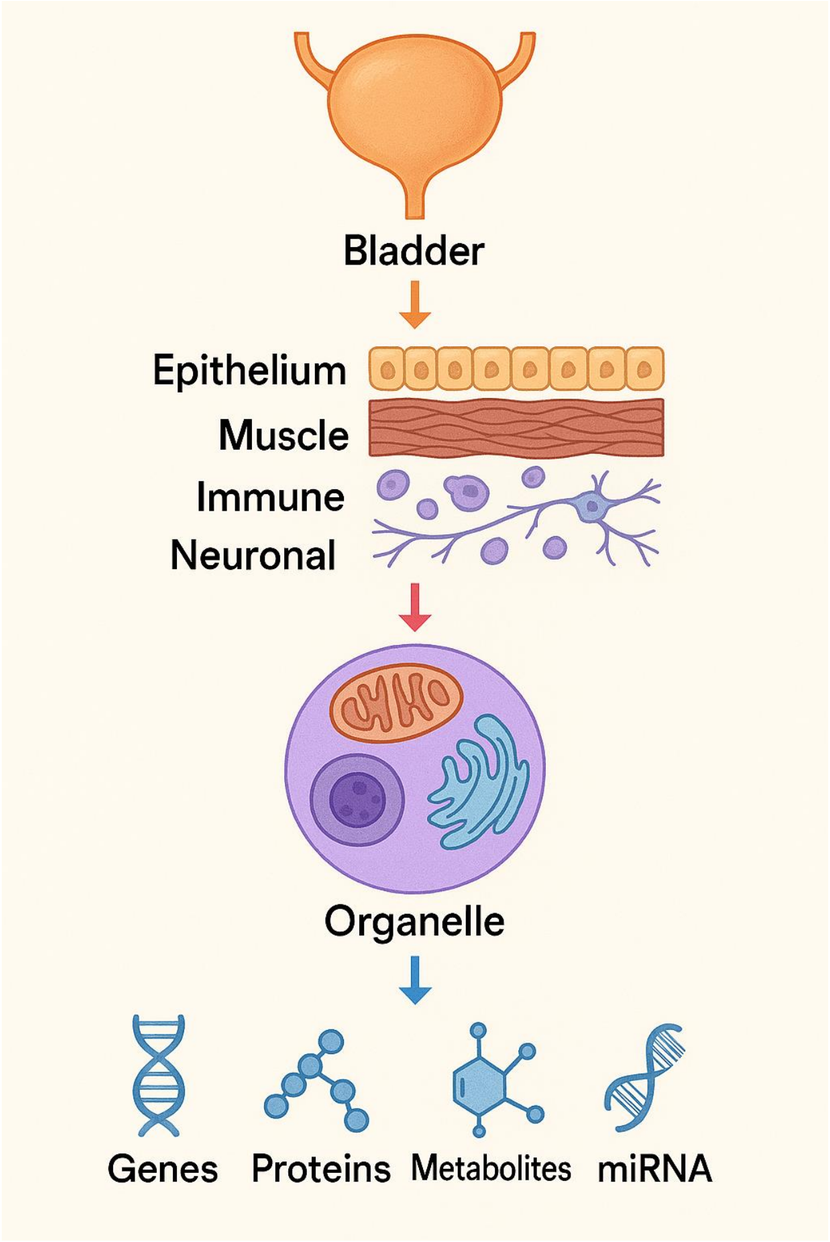
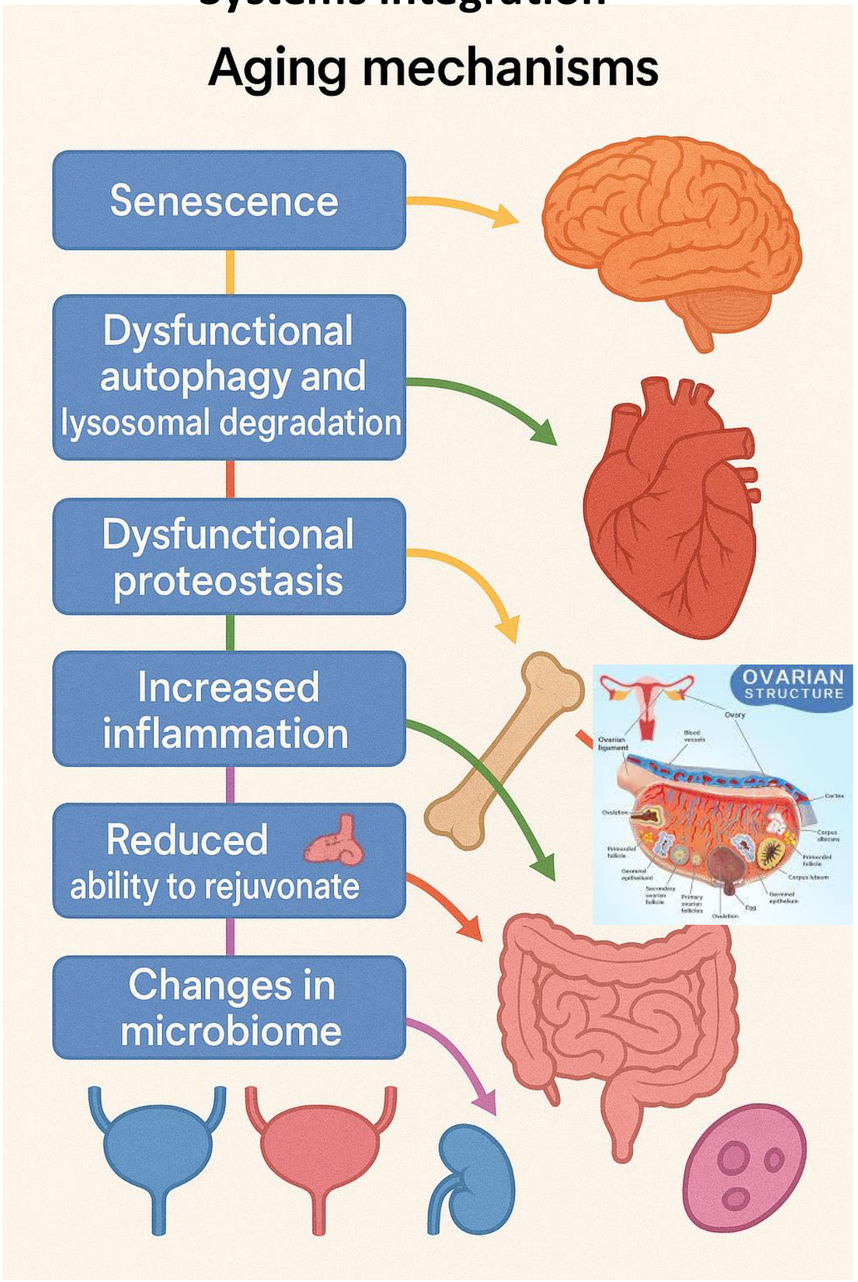




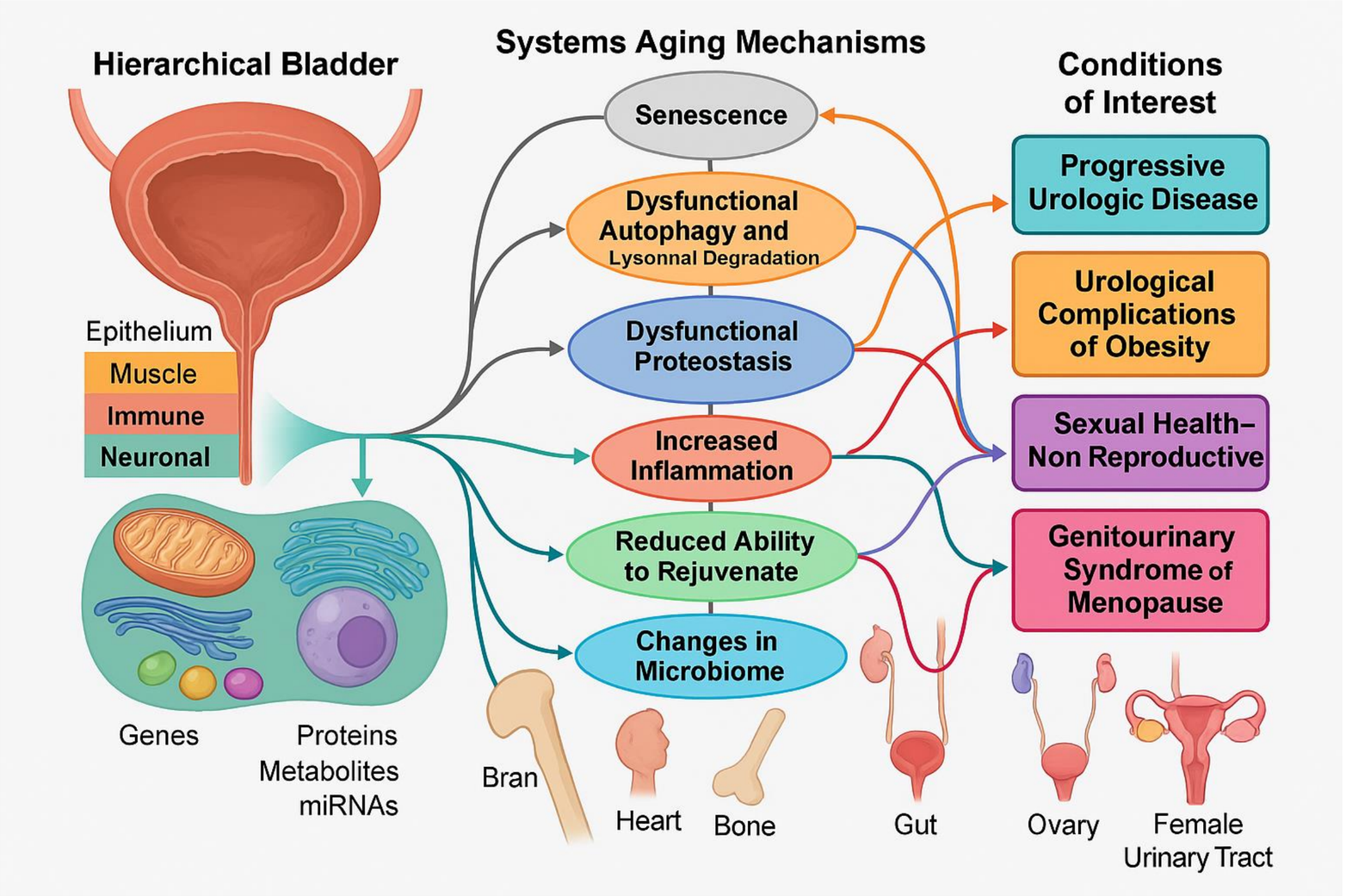


Functional output
AI/Machine learning approaches

Systems integration



- Progressive urologic disease
- Sexual health—non reproductive
- Urological complications of obesity
- Genitourinary syndrome of menopause
- Pediatric health



Introduction

Laura E. Pascal, PhD.

Research Assistant Professor

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- Pharmacology & Chemical Biology/DeFranco Lab

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Research Interests & Goals

Research Focus Areas

- Mitochondrial dysfunction in aging-related prostatic disease (and LUTS)
- ZC3H4 regulation of prostate homeostasis and disease
- ZC3H4/Restrictor complex function in prostate cell types

Primary Topics - Uro-Aging

- Adaptability and persistence of cells to aging process and how that contributes to prostate disease
- How do they contribute to disease?
- What can we do to inhibit/reverse this process and improve health?

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Key Expertise & Methods

Core Knowledge & Expertise

- Murine modeling of Aging, BPH and LUTS
- Mitochondrial function in cell lines
- Prostate cell biology and pathology, mouse and human

Skill Set

- Microscopy, Cell culture, siRNA
- Histology and prostate pathology (mostly mouse, some human)
- Transgenic modeling in mice

Access to Parkinson's Disease resources, no resources to share – yet!
University of Pittsburgh, Carnegie Mellon University

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Ongoing/Recent Projects

ZC3H4 Prostate Remodeling

Pending…

- ZC3H4 regulates mito fxn in prostate stromal cells, decreased in BPH
  - ZC3H4 kd/ko impact
  - So far: CI down, cell detachment, clustering, FN1 up
- NIDDK R01 PI: Laura Pascal
- Don DeFranco, Michael Jurczak, Uma Chandran, Jon Beckel (Pitt), Teresa Liu (UW)

Mito dysfxn in Aging/BPH - UW

End ~July 2026

- Mito fxn is altered in Aging and BPH
  - In vitro and in vivo modeling
  - So far: CI fxn is decreased, and targeting improves voiding in aged mice
- NIDDK R01: PI Will Ricke
- Will Ricke, Teresa Liu, Alexis Adrian (UW), Don DeFranco (Pitt)

Your Thoughts:
Major Knowledge Gaps in BPH/LUTS

Can BPH/LUTS be prevented?

- What are targetable mechanisms
- Comprehensive analysis of risk factors and impact on disease
- Orchestrated targeting, high throughput, animal models, physician and patient involvement

How to personalize treatment

- Stratification of disease AND patient
- Right target, right treatment, right patient
- Studies comparing treatment outcomes

Systems approach to BPH/LUTS

- Coordination of human data with bench models (AI?, NAM?)
- Centers with differing expertise and access, MD, PhD, patient, students
- Massive multi-institutional effort, partner with pharm?

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Introduction

Chad Vezina, PhD.

Professor & K12/R25 and TL-1? director

- University of Wisconsin-Madison
- Department of Comparative Biosciences

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Research Interests & Goals

Research Focus Areas

- Neuroimmune signaling in the urethra during infection and inflammation
- Mechanisms of non-malignant prostate disease
- Environmental influence on urinary health

Primary Topics

- Aging
- Neuro-urology
- Urobiome
- Mentored research training

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Key Expertise & Methods

Core Knowledge & Expertise

- Genetic approaches in mice to uncover mechanisms of urinary physiology
- Cellular and molecular mapping of the healthy and diseased urinary tract
- Developmental origins of urinary tract disease across the lifespan

Skill Set

- Mouse urinary physiology (muscle physiology, cystometry, cell excitation, cystometry, void spot assay, uroflowmetry, real-time imaging)
- Meso and microscale histology/pathology/imaging
- Training the next generation of researchers through short-medium term mentored research

Software for mouse urinary phenotyping
Veterinary (dog primarily) specimens, clinical data

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Ongoing/Recent Projects

Bedside to bench resources for lower urinary tract research

2022-2027

- Cellular anatomy of the urinary tract
  - Multiomic analysis of mouse and human urethra/bladder
  - Building new cell type specific cre Driver mice
- NIH/NIDDK RC2
- Doug Strand, UT Southwestern

Role of neuroendocrine cells in non-malignant urinary tract disease

2022-

- We seek to understand how neuroendocrine cells are activated and the role they play in UTI, BPH, SUI
- NIH/NIDDK U54
- J. Barasch (Columbia), M. Hadjifrangiskou (Vanderbilt), D. Strand (UT-Southwestern)

Your Thoughts:
Major Knowledge Gaps in the Field

Roles of the urethra in urinary disease

- How does urethra contribute to BPH/LUTD, SUI, Infection
- Collaborative teams: Neuro, Immunology, Physiology/Ion Channel, Genetics

Understanding how organ parts (cells) contribute to function of whole (organ)

- **Lots of new LUT cell populations identified by –omics – what is the role of each?**

* Pathology /tissue repositories, animal models, genetics, physiologists

Training gap Integrated hands-on training across non-cancer urology research areas for trainees at all stages (bootcamp like MDI kidney course?)

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