Segregating urinary phenome responses to microbes and other factors – new opportunities

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**Inflammation** \(\propto\) **presence of bacteria in human prostate**  
Hochreiter et al 2000 163:127-30

**Inflammation** \(\propto\) **progressive voiding dysfunction in men (incontinence, urinary retention, increased symptom index)**  
Torkko et al J Urol. 2015 194:454-61

**Bacterial** \(\propto\) **voiding dysfunction in mice (↑Frequency)**  
Lee et al PLoS One. 2015 10:e0116827  
Bell-Cohn et al AJP Renal. 2019 316:F682-F692

**Bacterial prostatitis** \(\propto\) **pain in mice**  
We can see ‘Active’ inflammation /infection but we cannot observe past events (especially subclinical).

Standardized tests in the clinic (mostly), but what about at the bench with research animals?
MAKE MOUSE VOIDING BEHAVIOR A QUANTITATIVE TRAIT

1. Start with a clean mouse cage.
2. Add filter paper.
3. Add the mouse and wait 4 hours.
MAKE MOUSE VOIDING BEHAVIOR A QUANTITATIVE TRAIT

Use Void Whizzard Software to analyze 12 features incl. spot number, size, distribution.
MAKE MOUSE VOIDING BEHAVIOR A QUANTITATIVE TRAIT

Lisa Abler, Royal Oakes, Kyle Wegner

Optimized for:

- Acclimatization time
- Mouse age
- Size and shape of cage
- Assay duration
- Cage type
- Time of day
- Consistency across institutions

Wegner et al and Hill et al, Amer J Physiol-Renal 2018
Collaboration Among UW-Madison, Beaumont Health, Beth Israel / Harvard P20 Center, Vanderbilt University
Rinse and Repeat

**Human**
- Voiding Diary
- Uroflowmetry
- Cystometry
- Urethrogram

**Mouse**
- Void Spot Assay
- Uroflowmetry
- Cystometry
- Contrast enhanced ultrasound
Current mouse urinary phenotyping assays can differentiate, but not diagnose.

Bjorling, Zeidel, Vezina, Hill et al AJP Renal 2015

Keil et al AJP Renal 2015
A mouse model of prostate inflammation

Ruetten et al. In Press AJP-Renal

Collaboration between UW-Madison, Columbia U. O’Brien Centers
Bacterial prostatitis does not always increase urinary frequency
Prostate inflammation causes different voiding patterns in mice. **Is this also true in humans?**

**IL1β overexpression**

- Uninflamed
- Prostate Inflamed

**E. coli CP1**

- Void Frequency
- Bladder Pressure

**E. coli 1677**

- Void Frequency

**E. coli UTI89**

- Spot count

*Lee, Bushman PLoS One 2015*

*Ruetten et al In press*

*Bell-Cohn, Thumbikat et al AJP Renal 2019*
Maybe, we need to change our approach?

Single features

Nuclei + Sm. Muscle + Fibroblast + Inflammatory

Many features

Kyle Wegner

Henry, Joseph, Strand et al
Aggregate Void spot assay data successfully classifies mice based on disease process

* Visit poster #47 for more information

- Hannah Ruetten, Gervaise Henry,
- Unpublished
- Collaboration between Vezina and Strand Teams
A phenomics approach for identifying LUTD mechanisms and stratifying populations

**Forward phenomics:**
Pathogen $\rightarrow$ phenotype

**Reverse phenomics:**
Phenotype to pathogen
Current
Thrishna Chathurvedula
Clara Cole
Olivia Fox
Thomas Peterson
Hannah Ruetten
Jaskiran Sandhu
Simran Sandhu
Brandon Scharpf
Anne Turco
Jonathan Zhu

Recent
Lisa Abler
Mark Cadena
Nicholas Girardi
Brett Mueller
Royal Oakes
Chelsea O'Driscoll
Kyle Wegner
Marlyse Wehber
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