

A Phenome-Based Approach for Characterizing Mouse Urinary Pathophysiologies

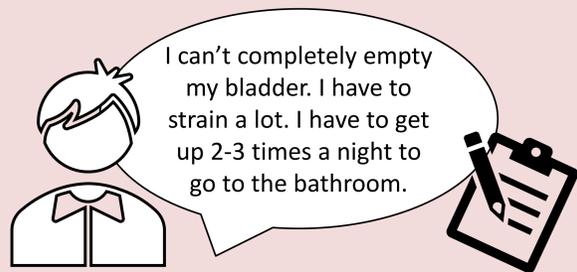
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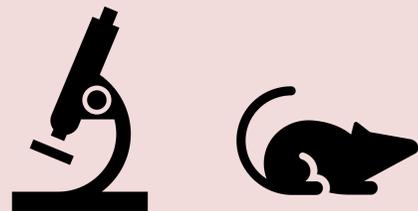
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In the clinic men are diagnosed with lower urinary tract symptoms after making an appointment with a doctor where they describe their symptoms and then fill our standardized surveys.

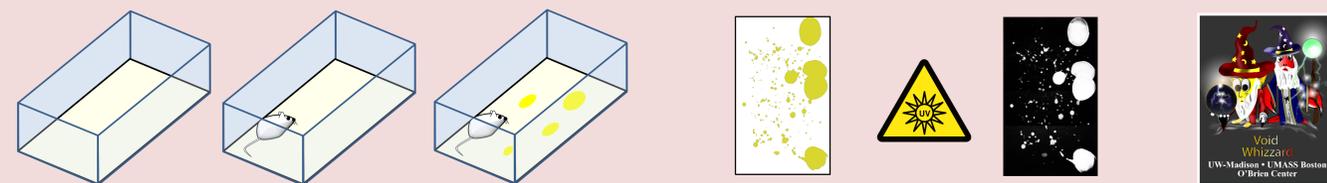


In the lab we use anatomic and histologic endpoints or tests such as CYSTOMETRY, UROFLOW, or VOID SPOT ASSAYS to assess urinary dysfunction. Using these tests we can detect changes in certain parameters, but we don't know which changes are truly pathologic, or which changes correspond to certain symptoms in men.

Research Questions

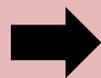
1. Using a single test for urinary dysfunction, the VOID SPOT ASSAY, can you distinguish mouse models of different pathophysiologies from one another?
2. What are the common VOID SPOT ASSAY features of diabetic diuresis, irritative urinary dysfunction, and obstructive urinary dysfunction?

Void Spot Assay



Select 3 different models of urinary dysfunction

- BTBR ob/ob model of diabetic diuresis
- T+E2 model of urinary obstruction
- *E. coli* UTI89 infection model of urinary irritation

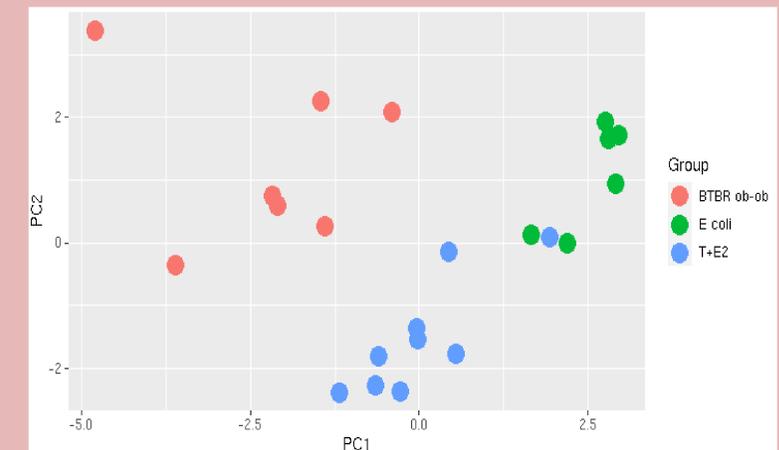


Obtain void spot assay results analyzed using Void Whizzard software for the three models we selected.

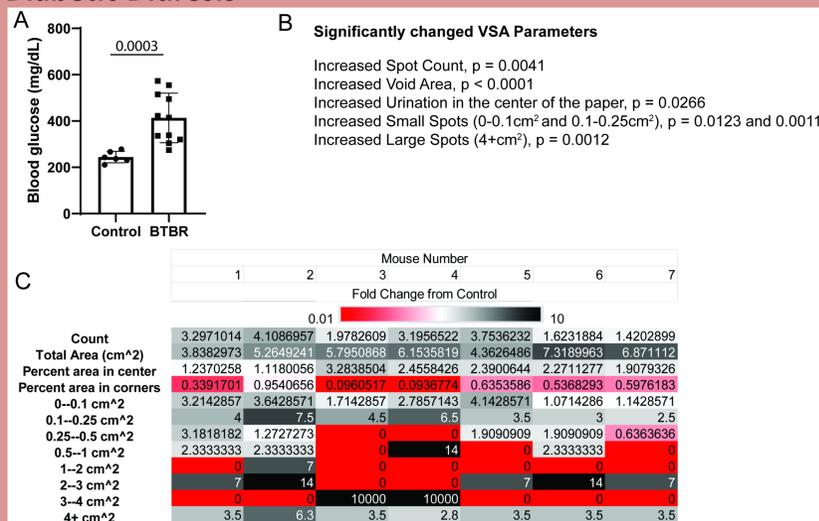
Normalize the endpoints of each treated mouse to control animals of the same age and background strain.

Multiple models of urinary dysfunction can be isolated using Void Spot Assay endpoints.

After normalizing the endpoint values to their respective controls the mice from the three different models of urinary dysfunction cluster separately on PCA analysis. (n = 6-9 per group)

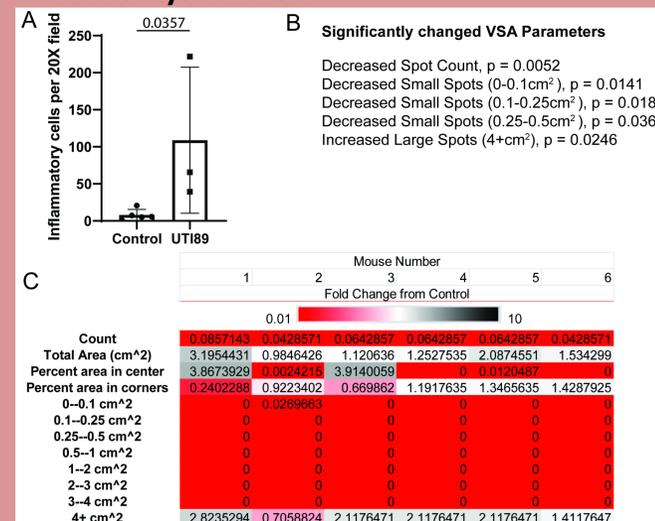


Diabetic Diuresis



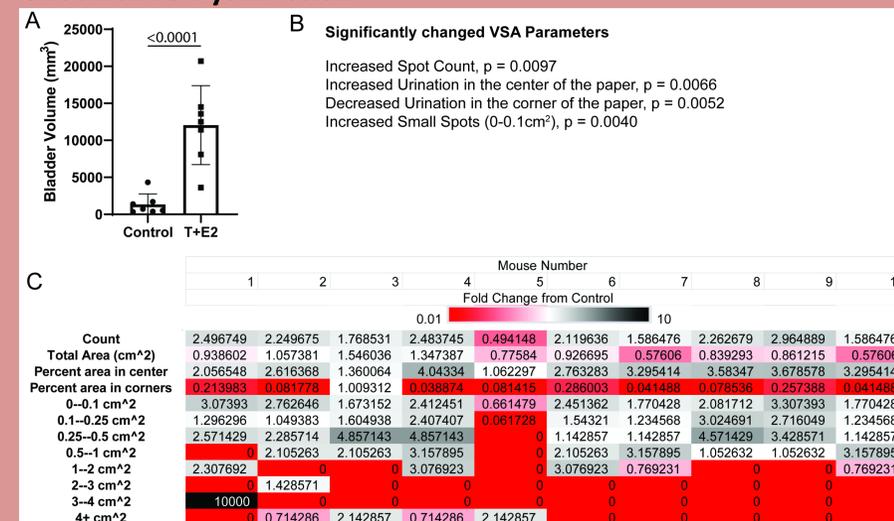
(A) Confirming hyperglycemia in BTBR ob/ob model. (B) VSA parameters that are significantly different from controls. (C) For each BTBR ob/ob mouse, fold changes from control in each VSA parameter.

Irritative Dysfunction



(A) Confirming prostatic inflammation in *E. coli* UTI89 model. (B) VSA parameters that are significantly different from controls. (C) For each *E. coli* UTI89 mouse, fold changes from control in each VSA parameter.

Obstructive Dysfunction



(A) Confirming urinary obstruction in T+E2 model. (B) VSA parameters that are significantly different from controls. (C) For each T+E2 treated mouse, fold changes from control in each VSA parameter.

Conclusions

- The void spot assay is a cheap and easy way to detect changes in urinary function in mice.
- It can be used to differentiate different types of voiding dysfunction (i.e. diabetic diuresis, irritative dysfunction, and obstructive dysfunction).
- The void spot assay can be used help to create better animal models and improve etiologic and therapeutic testing.