Immunohistochemical analysis of epithelial cell composition in the mouse prostatic urethra

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Abstract

Benign Prostate Hyperplasia (BPH) is non-malignant prostate enlargement that can result from epithelial cell proliferation, which constricts the urethra and causes lower urinary tract dysfunction (LUTD). The purpose of this study was to identify whether the proportion of luminal and basal cells change in aging and steroid hormone-induced (T+E2) mouse models of LUTD. Immunohistochemistry was performed on prostatic urethra tissue using basal cell marker p63. In urothelium, there was significantly higher percentage of luminal cells in aging (51.43%) versus young (31.84%, p=0.0125). There was an increasing trend in percentage of luminal cells in T+E2 (37.75%) versus UNT (31.84%, p=0.1115). This suggests that there is an increase in prostate luminal cells in the urothelium in LUTD.

Background

- Benign Prostatic Hyperplasia (BPH) is the non-malignant enlargement of the prostate that affects 80% of men aged 80 and older[1],with an estimated $4 billion per year in treatment costs[2].
- Symptoms include increased frequency, incomplete voiding, nocturia, and urinary retention.
- In the Ricke laboratory, we use mouse models to study BPH. The prostatic urethra region of the mouse lower urinary tract most closely resembles the human prostate (Figure 1). Changes in the prostate glands are similar to those seen in the prostate lobes[3].

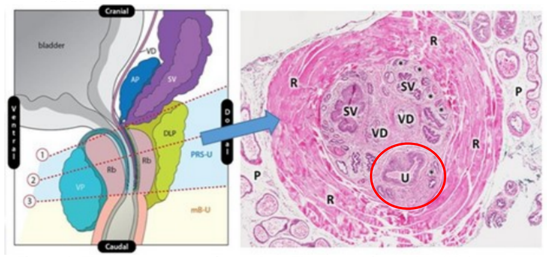

Figure 1: The mouse prostatic urethra. The prostatic urethra (U) is surrounded by prostate glands (*), which are connected to the prostate lobes (P) and encapsulated by the rhabdosphincter along with the seminal vesicle (SV) and vas deferens (VD). Only ducts surrounding the urethral lumen, shown in red, were included in analysis.

- BPH can result from epithelial cell proliferation, which constricts the urethra and causes lower urinary tract dysfunction (LUTD).
- Current therapies target luminal epithelial proliferation; however, approximately 8-10% of BPH specimens encompass basal cell proliferation which remains untargeted[4].

Materials and Methods

Tissue Selection

- Tissue sections were taken at the midpoint of the prostatic urethra from 3-month old untreated (UNT) (n=6), 24-month old UNT (aged mice, n=4), and 3-month old mice treated with testosterone and estradiol pellets for 1 month (T+E2, n=7).

Immunohistochemistry (IHC)

- Standard IHC protocol was performed to label p63-positive basal cells and counterstained with hematoxylin to label nuclei.
- Epithelial cells negative for p63 were counted as luminal cells.

Manual Analysis

- The percentage of basal and luminal cells in ventral prostate ducts surrounding the urethra and in the urothelium (Figure 1) was calculated and averaged for each experimental group.

Objective and Hypothesis

The purpose of this study is to identify whether the proportion of luminal and basal cells change in aging and steroid hormone-induced mouse models of LUTD.

I hypothesize that the luminal ratio will increase in the mouse prostatic urethra in LUTD consistent with the cellular composition observed in BPH.

Results

Epithelial cell composition in periurethral prostate glands does not change in LUTD.

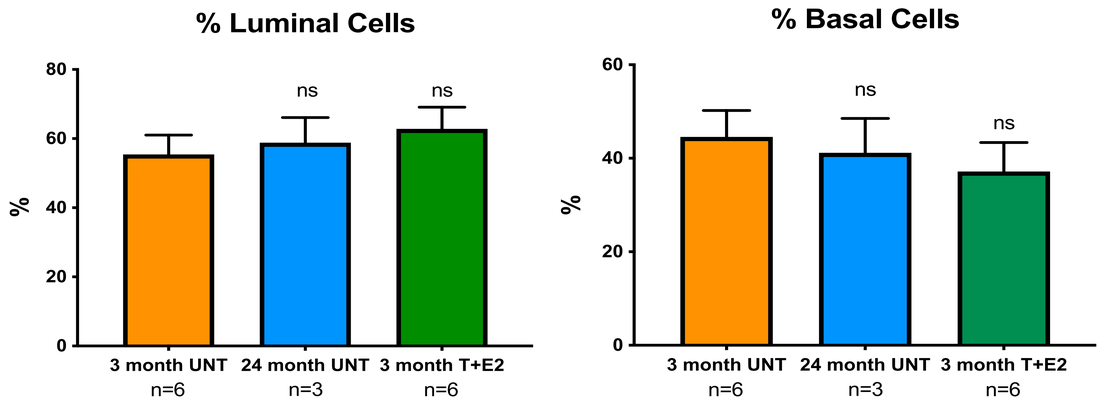

Figure 2: Percentage of epithelial cell types in prostate glands. There is a near-significant increase in the percentage of luminal cells in T+E2 (62.84%) versus UNT (55.40%, p=0.0554) mice. There is no significant difference in epithelial cell percentage between young and old mice (*p*=0.467). Student's t-test was used to determine if cell percentages were different from control in either of the two models. Error bars show SD.

Epithelial cell composition in urothelium is different in aging but not in hormone-induced LUTD.

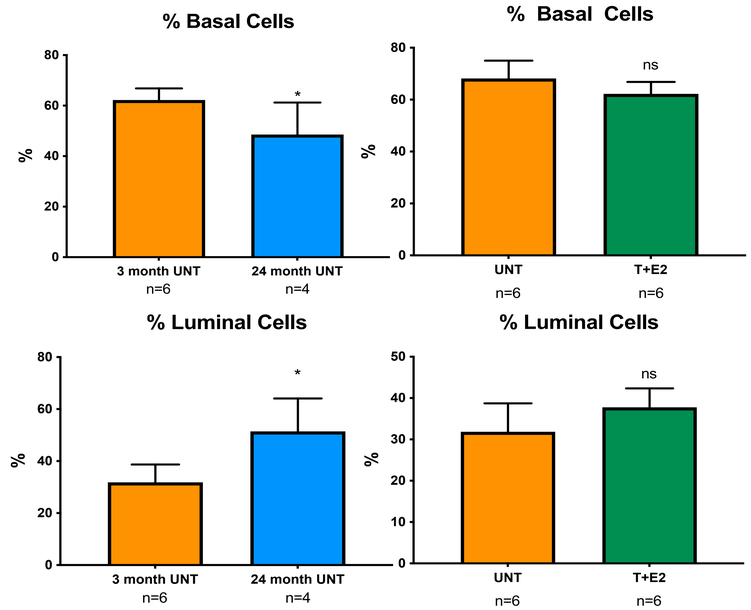

Figure 3: Percentage of epithelial cell types in urothelium. There is a significantly lower percentage of basal cells in 24 month mice (48.57%) in comparison to 3 month mice (68.16%, p=0.0383). Likewise, there is a significantly higher percentage of luminal cells in 24 month mice (51.43%) in comparison to 3 month mice (31.84%, p=0.0125). There was an increasing trend in percentage of luminal cells in T+E2 treated (37.75%) versus un-treated (31.84%, p=0.1115). Error bars show SD.

Results (cont.)

Number of periurethral prostate glands does not change in LUTD.

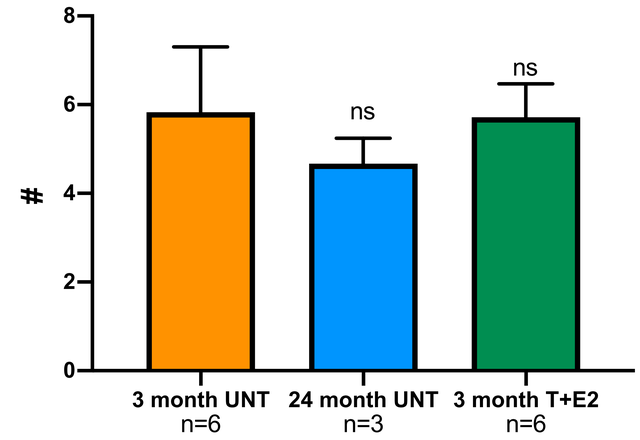

Figure 4: Number of prostate glands surrounding the urethral lumen. There is no significant difference in the number of prostate glands between young and old mice (p=0.2389) or untreated and T+E2 treated mice (p=0.8544). Error bars show SD.

Discussion

- Results suggest there is an increase in prostate luminal cells in the urothelium in mice with LUTD. This could be an indication of luminal cell hyperplasia.
- Basal cells are present in mouse prostate glands, suggesting that glands in the prostatic urethra have similar histology to mouse prostate lobes.
- We did not identify basal cell hyperplasia in either LUTD models indicating the need for the development of new strategies to study this pathological phenotype.

Future directions

- Repeat experiment with larger sample size.
- Expand region of interest to entire prostatic urethra, and analyze difference in prostatic ducts derive from different prostatic lobes
- Perform IHC with proliferation markers.

References

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