

Rapid Tissue Collection for Consistent Detection of Prostate Markers in female Urethral Tissue

Britt Haller^{1,2,3}, Elena Takano¹, Stephen Fox¹, Noel Woodford⁴, James Brock², Helen E O'Connell^{2,3}

¹ Peter MacCallum Cancer Institute, ² University of Melbourne, ³ Department of Urology, Western Health, ⁴ Victorian Institute of Forensic Medicine. Email: britt.haller@wh.org.au



Epworth
Research

Introduction

Female urethral adenocarcinoma is a rare and highly malignant disease. It is often diagnosed at an advanced stage which limits treatment to major surgical excision in most cases. Though not well characterized, some of these tumours appear to arise in glands around the urethra, referred to as Skene's glands¹, and may express prostate specific antigen (PSA) and prostatic specific acid phosphatase (PSAP). Post-mortem studies on normal tissue have identified intermittent positivity in approximately half of subjects². This project examined the expression of PSA and PSAP in normal female urethral tissue collected and fixed within a rapid autopsy program; Cancer Tissue Collection after Death (CASCADE). The objective was to establish if PSA and PSAP expressing structures can be reliably identified and to allow further characterisation of the labelled structures. This could allow greater understanding of their function in normal tissue and provide clues to improved detection and treatment strategies for urethral adenocarcinoma, including chemotherapeutic targets.

Aims

To clarify the anatomy, distribution and type of glands in female peri-urethral tissue, to aid in understanding of urethral cancer which may help in refining chemotherapeutic targets.

Methodology

The urethra and surrounding tissue was obtained from nine donors in a post mortem setting within 4-12 hours, formalin fixed for 30-80 hours and divided into 5mm transverse slices. Representative sections from each slice were immunolabeled for PSA (Rabbit A0562, DAKO; 1:5000) or PSAP (Rabbit A0627, DAKO; 1:5000). Labelling was detected with Envision FLEX/HRP (Dako), visualised with 3-3'-diaminobenzidine, counterstained with haematoxylin and Scott's solution and viewed under a light microscope.

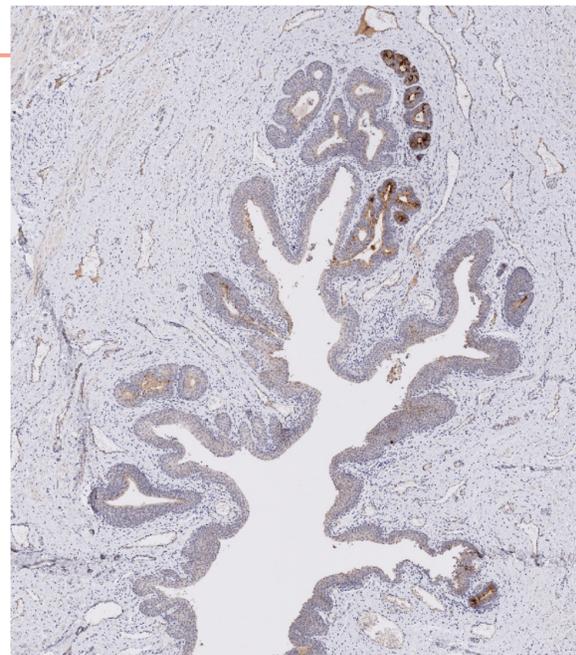


Figure 3. PSAP expression in proximal urethral tissue.

Results

Immunolabeling for PSA was observed in the urethra of six of nine urethras, in the distal urethra, defined as within 2 cm of the distal urethral meatus. An example of the location of PSA staining relative to the urethral lumen is shown in figure 1 (below). In representative sections from each block along the urethra, PSA positive structures were observed to be discrete from and not continuous with the urothelial lining. All PSA staining structures also expressed PSAP, shown in figure 2 (below). In this study PSAP was also observed in the proximal urethra of all nine samples, appearing continuous with the urothelial lining. The proximal urethra was defined as 3-4cm from the distal urethral meatus. An example of PSAP staining in the proximal urethra, showing its proximity to the urethral lumen, is shown in figure 3 (left).

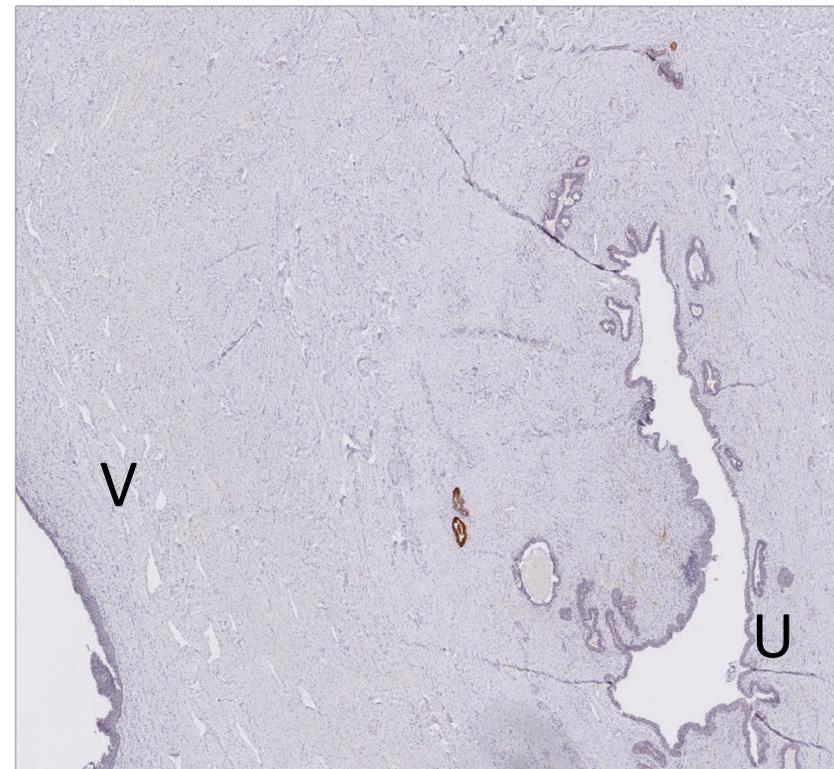


Figure 1. PSA positive gland in tissue surrounding distal urethral lumen (U), in relation to anterior vaginal wall epithelium (V).

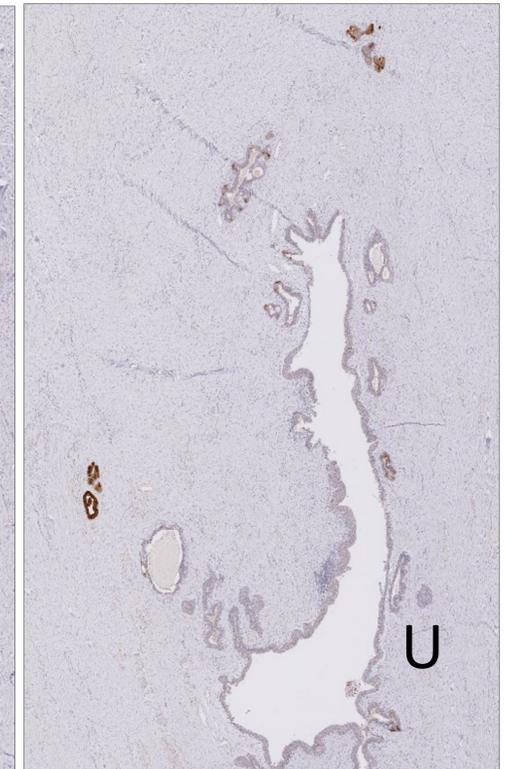


Figure 2. The same section as in Figure 1 showing PSAP expression surrounding urethral lumen (U)

Conclusions

In this project, detection of PSA and PSAP expressing glandular structures was more consistent than observed in previous studies. This was likely due to rapid tissue collection and fixation enabled by the CASCADE program, and/or the specific immunohistochemistry protocol and highly sensitive detection system. To our knowledge, the identification of PSAP labelled structures in the proximal urethra has not been reported in previous studies. These findings hold promise for reliable characterisation of the anatomy of the female urethra including structures implicated in female urethral adenocarcinoma.

References

1. Skene A. Anatomy and pathology of two important glands of the female urethra. *Am J Obstet Dis Women Child.* 1880;13:265-70.
2. Dietrich W, Susani M, Stifter L, Haitel A. The human female prostate-immunohistochemical study with prostate-specific antigen, prostate-specific alkaline phosphatase, and androgen receptor and 3-D remodeling. *J Sex Med.* 2011;8(10):2816-21.