

## HIGHER EXPRESSION OF PDE5 IN THE ANTERIOR FIBROMUSCULAR STROMA OF THE HUMAN PROSTATE THAN IN OTHER GLANDULAR ZONE

### Hypothesis / aims of study

Phosphodiesterase type 5 (PDE5) inhibitors have been proven as effective pharmacotherapy for men suffering from erectile dysfunction and also for men suffering from lower urinary tract symptoms (LUTS). The distributions of PDE5 are analysed in human genitourinary tracts such as the bladder, prostate, and urethra [1]. The higher expression of PDE5 in the bladder was reported than in the prostate [1]. Thus, more detailed analysis of PDE5 distribution according to the zonal anatomy of the prostate could enhance understanding of the effective targeting tissue of PDE5 inhibitors. Interestingly, possible functional contribution of the anterior fibromuscular stroma (AFMS) of the human prostate to the urinary function has been reported [2, 3]. The peculiar innervations pattern was seen in the AFMS compared with the other glandular zone [2]. The objective of this study is to evaluate the expression of PDE5 in the AFMS and to quantitatively compare that in the other glandular zone or the bladder neck using immunohistochemistry with computer-assisted image-analysis technique.

### Study design, materials and methods

Ten human prostate and bladder specimens were obtained from cystoprostatectomy for bladder cancer. The paraffin serial sections were used for H&E stain and the immunohistochemistry for PDE5 antibody. Selected fields were analysed from the AFMS, the peripheral zone (PZ), and the bladder neck in order to quantify. The ratio of immunoreactive area of PDE5 to the area of smooth muscle in H&E stain was calculated using computer-assisted image analysis system.

### Results

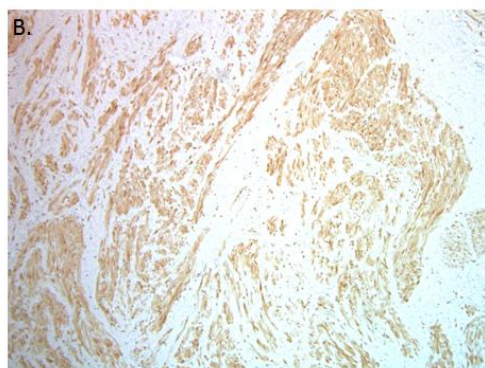
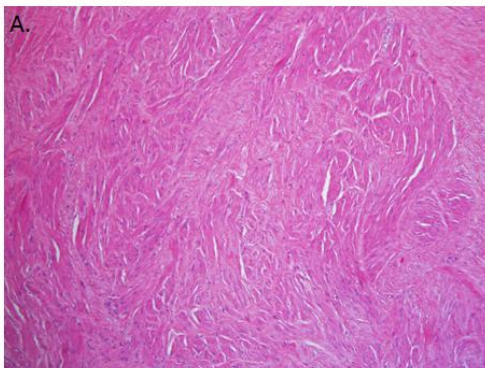
PDE5 immunoreactive area was seen in smooth muscle bundles in each region (Figure 1). The AFMS and the bladder neck indicated intense PDE5 immunostaining. The higher expression of PDE5 was observed in the AFMS compared with the PZ. PDE5 immunoreactive area in the transition zone seemed to be intermediate between the AFMS and the PZ although it was difficult to quantify due to large variability of smooth muscle component and glandular component in the transition zone. Image analysis showed that the average ratio of immunoreactive area of PDE5 to the area of smooth muscle in H&E stain was 91.9% in the AFMS, 68% in the bladder neck and 45.0% in the PZ, respectively. There was the significant higher expression of PDE5 in the AFMS than in the PZ ( $p < 0.05$ ). There was no significant difference of PDE5 expression between the AFMS and the bladder neck.

### Interpretation of results

The higher expression of PDE 5 was identified in the AFMS than in the PZ. The results of this study suggested that the AFMS could be the prostatic target tissue of PDE5 inhibitors in pharmacotherapy for LUTS.

### Concluding message

To our knowledge, this is the first study to show the higher expression of PDE5 in the AFMS than in other glandular zone. AFMS could be the main target tissue of PDE5 inhibitors in the human prostate.



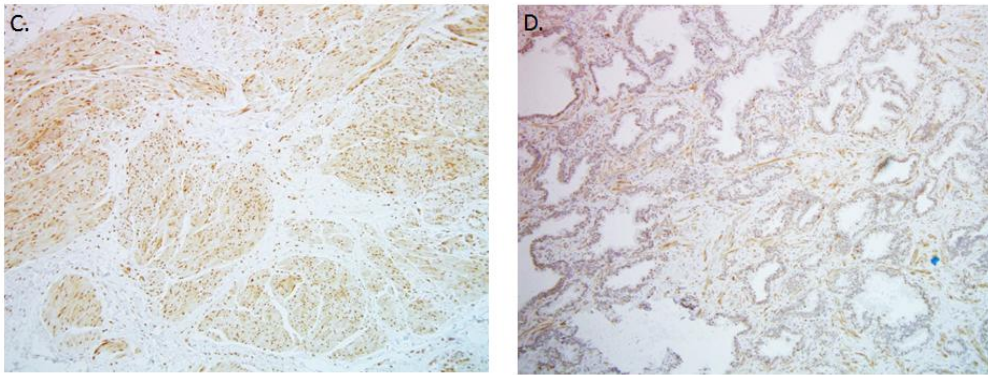


Figure.1  
 H&E stain in the AFMS(A) shows abundant smooth muscle bundles. Figure B, C and D are images of immunohistochemistry for PDE5 antibody in each region. Smooth muscle bundles in the AFMS (B) as well as bladder neck (C) show intense PDE5 immunopositivity. PZ (D) shows relatively scanty PDE5 immunoreactivity. (magnification 100X)

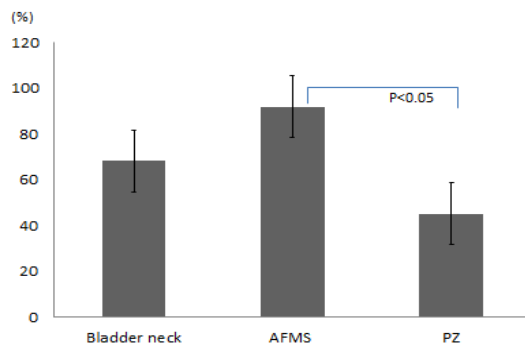


Figure. 2  
 The ratio of PDE5 immunoreactive area to smooth muscle area calculated by computer-assisted image analysis

References

1. The Journal of sexual medicine. 2010;7(1 Pt 1):59-69.
2. The Prostate. 2001;48(4):242-7.
3. Ultrasound in medicine & biology. 2004;30(5):575-81.

Disclosures

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