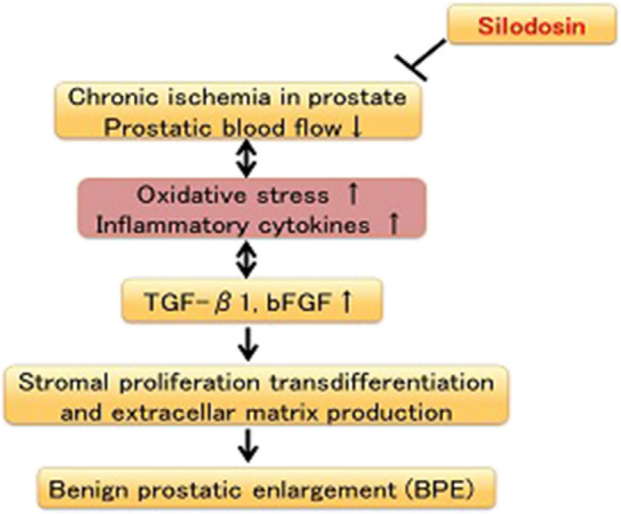

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MP31-03

DIFFERENCES IN THE CONTRACTILITY OF HUMAN ISOLATED PROSTATIC URETHRA TO OXYTOCIN AND NOREPINEPHRINE IN BENIGN PROSTATIC HYPERPLASIA: POTENTIAL ROLE OF OXYTOCIN IN BPH.

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INTRODUCTION AND OBJECTIVES: Previously we have demonstrated that oxytocin (OT) can cause contraction of human prostate through oxytocin receptors. The aim of the present study was to evaluate whether OT can also produce contraction of human isolated prostatic urethra and determine whether this response is mediated by specific OT receptors using the selective oxytocin receptor antagonist epelsiban.

METHODS: Prostatic urethra was obtained from 8 patients (67 ± 3 years old) undergoing cystoprostatectomy for bladder cancer or prostatic adenomectomy for BPH. Strips were mounted under 1 g of initial tension. After a 60 min equilibration, strips were exposed to 30 μM norepinephrine (NE) to determine tissue viability. After wash-out and 60 min of re-equilibration, epelsiban (30, 100 and 300 nM) or its solvent (distilled water) were incubated for 60 min. Then, a single concentration of oxytocin (1 μM) was tested. In different strips, tamsulosin (10 nM) or its solvent (distilled water) were incubated for 45 min before each addition of NE (0.1-0.3-1-10-30 μM), added in a non cumulative manner

RESULTS: In preliminary experiments it was determined that cumulative concentration response curves to OT and NE were not possible due to desensitization. In subsequent experiments, the magnitude of contractions induced by 1 μM oxytocin were 11.68 ± 2.68% and 27.21 ± 7.02% (of contractions to 30 μM NE) for strips from cancer and BPH patients respectively ($p = 0.0537$). Epelsiban inhibited contractions induced by 1 μM OT. However due to the large variability in the response to OT (particularly between the two patient groups), coupled with the low n number (n=5), effects did not reach statistical significance.

NE (0.1 − 30 μM) added non-cumulatively, induced concentration-dependent contractions of human isolated prostatic urethra. Interestingly the magnitude of contractions induced by 30 μM NE were different between the two patient groups, however it was the reverse profile in comparison to OT (1.77 ± 0.18 g and 0.99 ± 0.16 g from bladder cancer and BPH patients respectively, $p<0.01$). Tamsulosin (10 nM) abolished the contractile effect of NE.

CONCLUSIONS: This is the first demonstration of a contractile effect of OT in human prostatic urethra through specific OT receptors. In addition, OT appears to produce larger responses in tissue from BPH patients.

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MP31-04

CD8+ T CELLS PROMOTE PROLIFERATION OF BENIGN PROSTATIC HYPERPLASIA EPITHELIAL CELLS IN THE CONDITION OF LOW ANDROGEN

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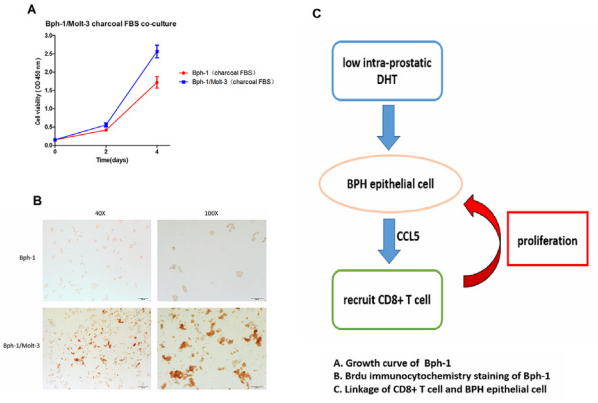
INTRODUCTION AND OBJECTIVES: Clinical studies suggested that androgen might be associated with infiltrating T cells in prostate of benign prostatic hyperplasia (BPH) patients. Previous studies of our laboratory (data from 64 cases of BPH patients with/without finasteride treatment) have shown that low intra-prostatic dihydrotestosterone (DHT) induced the BPH epithelial cells to recruit CD8+ T cells via modulation of CCL5 secretion. However, the consequences of CD8+ T cells towards prostate tissues remained unclear. Therefore,the present study aimed to investigate the effects of CD8+ T cells on BPH epithelial cells in low DHT condition.

METHODS: In vitro co-culture system was used to detect impacts of CD8+ T cell line–Molt-3 cells on the BPH epithelial cell line–Bph-1 cells in the low level of DHT condition (medium was treated with 10% charcoal fetal bovine serum). Then during a 4-day co-culture, the Bph-1 cells growth status were detected by CCK8 assay and Brdu immunocytochemistry staining assay. Meanwhile, the expression of Proliferating Cell Nuclear Antigen (PCNA) was analyzed in Bph-1 cells by western blot assay.

RESULTS: It's observed from CCK8 assay showed that Molt-3 cells could significantly promote Bph-1 cells proliferation in the low DHT condition after the 4-day co-culture compared with Bph-1 cells cultured alone on day 2 and day 4 (day 2: $p<0.01$, day 4: $p<0.01$). Furthermore, the Brdu immunocytochemistry staining assay was also showed that the Brdu expression was higher in Bph-1 cells which co-cultured with Molt-3 cells. Finally, the western blot results confirmed that PCNA was up-regulated in Bph-1 cells after co-culture with Molt-3 cells in the low DHT condition.

CONCLUSIONS: In conclusions, our findings suggested that infiltrating CD8+ T cells could promote the proliferation of BPH epithelial cells in low androgen condition which might provide new insights for a new therapeutic that anti-inflammation therapy combined with anti-DHT therapy in patients with BPH may be warranted in the future.



Source of Funding: none