Androgens play critical roles in epithelium proliferation in BPH not normal adjacent

**Background:** The prostate is an androgen-sensitive organ composed of glandular cells embedded in a surrounding stroma, and stromal AR and androgens play critical roles in prostatic development and adult homeostasis. Our preliminary data showed the AR signaling are playing essential role in the proliferation of epithelial cells in BPH, but not stromal cells from normal adjacent prostate NAP. Furthermore, androgens significantly increased the proliferation of prostatic epithelial cells in patient derived explant (PDE) of BPH but not the paired normal epithelial cells. However, the underlying mechanisms of this phenomenon are still unknown.

**Method:** Tissue from human BPH specimens obtained through BPH patients undergoing simple prostatectomy for symptomatic BPH. PDE were utilized to evaluate the androgen impact in BPH tissue and paired normal adjacent tissue. Proliferation, cytokines and androgen-responsive genes were validated in clinical BPH specimens and paired normal prostatic specimens via iHC and qPCR.

**Results:** The tissue could maintain original structure and AR signaling in PDE model at least 4 days. PDE models showed that androgen could impact epithelium proliferation in BPH tissue, but not NAP tissue. Stromal cells of the BPH tissues secreted higher level of CCL family proteins (CCL8, CCL11, CCL13 and CCL28), CXCL proteins (CXCL6, CXCL12), interleukins (IL6, IL7 and IL12), and growth factors than those from the paired normal adjacent tissues. RNA sequencing data showed that several cytokines and growth factors were upregulated in BPH-stromal cells after androgens stimulations but not in normal adjacent stromal cells, which are confirmed by qPCR.

**Conclusions:** These findings suggested that PDE model were able to utilize as a predominant model to mimic the vitro environment. Androgens have been shown to increase the proliferation of epithelial cells in PDE model. Androgens have been shown to influence the expression of several genes including CXC and interleukins in BPH stromal cells, but not normal adjacent stromal cells. Our results suggest that androgen signaling in BPH stromal cells is dysregulated and could contribute to prostatic epithelial growth and provide a strong foundation to elucidate the mechanisms of androgen-dependent stromal regulation of epithelial cell growth in BPH.

Androgens stimulate epithelial proliferation in the presence of conditioned medium from BPH stromal cells

The proliferation in epithelial cells and stromal cells of human prostatic tissue in BPH and normal adjacent

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