Title: *SRD5A2* Promoter Methylation is associated with Estrogen Receptor β in BPH

Background: Steroid 5α-reductase type II (SRD5A2) is the predominant enzyme responsible for prostatic development and growth. We found that expression of SRD5A2 in the prostate is variable, and that one-third of prostate tissue samples from BPH patients do not express SRD5A2. We demonstrated that the absence of SRD5A2 expression is associated with *SRD5A2* methylation in the promoter region. We also demonstrated that there is an "androgenic to estrogenic switch" when SRD5A2 is absent in the prostate gland. Here we wished to identify if *SRD5A2* methylation in the promoter region effects on the expression of estrogen receptors (ERs). **Methods:** We used human prostatic stromal and epithelium cells, and prostate specimens collected from patients who underwent transurethral resection of the prostate (TURP). The expression of ERα and ERβ was determined by immunohistochemistry and semi-quantified with immunoreactive scores. Genome DNA was extracted and *SRD5A2* promoter methylation was determined with DNA methylation-specific PCR. The level of *SRD5A2* promoter methylation was correlated to ER expression. **Results:** Both of ERα and ERβ were expressed in prostatic stroma and epithelia compartments. In cultured prostatic stromal and epithelium cells, ERα was expressed in both cytoplasm and nuclei, and ERβ was only expressed in the nuclei. Six out of twenty patients had *SRD5A2* hypermethylation at the promoter region, which was associated with the expression of ERβ in the epithelia compartment ($p=0.023$). **Conclusions:** ERα and ERβ co-localize in human benign prostatic tissue. Specifically, ERβ is expressed in the nuclei of both the prostatic stromal and epithelium cells. *SRD5A2* promoter methylation is associated with the expression of ERβ. Targeting the estrogenic signaling may serve as an effective treatment strategy in subset of *SRD5A2* hypermethylation and ER-sensitive BPH patients.