Title: Chromatin accessibility patterns reveal divergent genomic action of androgen receptor in nonmalignant prostate epithelial cells and prostate cancer cells

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Abstract

Androgen receptor (AR) is a nuclear receptor that binds DNA sequence at androgen response elements (ARE) following testosterone (DHT) stimulus. During transformation, the role of AR changes from regulation of cell differentiation to promotion of cell growth and division. Using assay for transposon accessible chromatin (ATAC) for benign and malignant prostate epithelial cells treated with DHT, we characterized the regulatory elements where accessibility changes following AR activation. We found that the pattern of chromatin accessibility is different between nonmalignant and cancer cells for unstimulated cells, and that the differences in accessibility are accentuated following DHT stimulus. Most accessibility changes in both cell types occur outside of promoter regions.

The patterns of chromatin accessibility in the models resembles the respective clinical diseases as the nonmalignant cells have highest signal in the open regions specific for benign prostatic hyperplasia, whereas the cancer cells have highest signal in the open regions of the primary cancer or castration resistant prostate cancer specific sites. Binding sites of multiple prostate TFs were enriched in the differentially accessible regions between DHT levels in each cell type, while ARE is the only TF binding motif with significant and consistent enrichment in TF footprinting analysis.

To conclude, our results show that AR binding has distinct effects on the chromatin accessibility landscape of nonmalignant and cancer cells with the potential for divergent effects on regulation of gene expression.