「前立腺がん進行におけるアンドロゲンシグナルの役割
／Role of Androgen Signaling in Prostate Cancer Progression」

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Androgen signaling is critical for development and progression of prostate cancer (PC). Recent studies revealed that this signaling is also important in advanced castration-resistant PC (CRPC). To clarify androgen signaling network, we isolated genome-wide androgen target genes in PC cells. They include APP, 14-3-3zeta, ArfGAP3, ABHD2, TACC2, G3BP2 and COBLL1, isolated by ChIP-clonig, ChIP-chip, and ChIP-seq analyses combined with transcriptome analyses. The integrated high-throughput genome analyses provide useful information for mechanisms of androgen action and potential diagnostic and therapeutic targets in PC including CRPC. Especially, these analyses revealed numerous noncoding RNAs such as microRNAs (miRNAs) and long noncoding RNAs (lncRNAs). We identified an androgen-responsive nuclear lncRNA, CTBP1-AS, located in the antisense region of CTBP1. CTBP1-AS promotes both hormone-dependent and castration-resistant tumor growth by epigenetic mechanisms, collaborating with RNA-binding protein PSF. Notably, PSF is involved in PC progression, promoting abnormal splicing such as production of AR-variants, such as AR-V7. Moreover, we will discuss about novel androgen-responsive genes involved in growth and progression of CRPC and neuroendocrine PC (NEPC). These molecules and functions will be novel targets for new diagnostic and therapeutic strategies of cancer.

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