GS02-6 **Identification of critical AR-V7 target genes and investigation of novel strategy for castration resistant prostate cancer**

○ Masahiro SUGIURA[1,2], Hiroaki SATO[1,2], Naohiko ANZAI[3], Tomohiko ICHIKAWA[1], Atsushi KANEDA[2]

[1]Dept Uro, Grad Sch Med Chiba Univ, [2]Dept Mol Oncol, Grad Sch Med, Chiba Univ, [3]Dept Pharm, Grad Sch Med, Chiba Univ

In prostate cancer, AR is a type of nuclear receptor that is activated by binding testosterone and then migrates into nucleus. The lignd stimulated AR affects prostate cancer progression by regulating the transpription of AR target genes. Although hormone therapy is effective at first to control cancer growth, most patients eventually relapse castration resistant prostate cancer (CRPC). Aberrant expression of splicing variant of androgen receptor (AR), called AR-V7, is one of the mechanisms for CRPC, regulatory function of AR-V7 are mostly unknown. Here we performed comprehensive analysis of transcriptome and epigenome by RNA-seq and ChIP-seq for H3K4me1, H3K4me3, H3K27ac, and AR/AR-V7, using LNCaP as primary prostate cancer cell line, and CRPC cell line expressing AR-V7 in the absence of androgen. While AR required testosterone to migrate into nucleus, AR-V7 could translocate into nucleus without testosterone. Whereas most of the AR-V7 target regions could be commonly activated by AR, 22 regions were identified as AR-V7 specific target regions. Knockdown of AR-V7 decreased cell proliferation, with repression of genes nearby those common and specific AR-V7 target regions. Among these candidates of critical AR-V7 downstream genes, we identified two genes contributing to cell proliferation and significantly upregulated in clinical CRPC tissues with high AR-V7 expression. One of the two genes is a trasmembrane protein called VB1. Specific inhibitors against VB1 complex caused decreased cell proliferation through apoptosis. This inhibitors may have a potential as a therapeutic strategy for CRPC.