GS02-3 **A model of treatment strategy using epigenetic inhibitors (Prostate Cancer)**

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Accumulation of both genetic and epigenetic aberrations are related to cancer tumorigenesis and acquisition of treatment resistance. In epigenetic aberrations, activation of enhancers, which are elements regulating transcription of neighboring genes, is reported to induce upregulation of oncogenes in several cancers. Among enhancers, furthermore, super-enhancers defined by clusters of master transcription factor or acetylated histones are known to regulate cell identity and cell fate even in cancer cells.

In prostate cancer (PC), enhancers are activated by androgen receptor (AR), and androgen deprivation therapy (ADT) is effective in first. However, most tumors acquire ADT resistant state called as castration resistant PC (CRPC). In CRPC, while androgen or AR independent activations of cancer related genes are reported in many papers, resistant mechanisms relating to enhancer aberrations or super-enhancers are still remain unclear.

Utilizing ADT sensitive PC cell line LNCaP and its derivative CRPC cell line LNCaP95, we performed ChIP-seq as follows: promoter mark; H3K4me3, enhancer mark; H3K4me1, active mark; H3K27ac, reader of acetylated histones; BRD4, RNA polymerase II, etc., and then defined super-enhancers by clusters of H3K27ac. Furthermore, we analyzed alterations of gene expression comprehensively by RNA-seq. Integrative analysis of these epigenome and transcriptome revealed mechanisms of regulating enhancers and super-enhancers in both cell lines, resulting in our investigation of a therapeutic model using epigenetic inhibitors for PC.