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Introduction & Objectives: Prostate cancer (PCa) is the most frequently diagnosed cancer among male. The incidence and mortality rate of prostate cancer (PC) has been rapidly increasing in the past 10 years in Taiwan. Patients with PCa that recurred after local therapy or metastasized usually respond to androgen deprivation therapy (ADT) initially. However, most patients experience disease progression and become castration resistant prostate cancer (CRPC). There are few existing medications including enzalutamide and abiraterone acetate have been used to treat the CRPC. Resistance to these novel agents occurred and eventually patient will die of the cancer progression. The mechanism(s) involved in the development of the drug-resistant CRPC is not fully elucidated.

Results: Here, we have established the enzalutamide and abiraterone acetate resistant LNCaP cell lines, LNCaP EnzR and LNCaP AbiR, to explore the resistant mechanisms of CRPC. Our results revealed that the proliferation and invasion ability of LNCaP-EnzR and LNCaP-AbiR cell lines were higher than its LNCaP-parental cell. Compared to LNCaP-parental cell, the expression of neuroendocrine-related genes, such as NSE were activated in LNCaP-EnzR and LNCaP-AbiR cells. Also, the LNCaP-EnzR and LNCaP-AbiR cells had higher tumorigenicity in vitro and in vivo. RNA-seq analysis showed aberrant gene expression that may played an important role in the resistant mechanisms. There were up-regulated genes including HGF, PDK4, MUC13, ADIRF, CNN3, RPL39L, DKK1, SSX3, CFC1B, CFC1, LOC102723360, SV2A, KLK1, SUSP3, CGB2, METTL7B, HSPB6, CNTN1, RIBC2, LPL and down-regulation genes GAGE12G, RNU6-2, RNU6-9, GAGE4, GAGE2C, RAB25, GAGE5, SMN2, GUSBP9, EIF1AY, UGT2B11, PLA2G2A, DDX3Y, RHOD, DIO3, VCX, UGT2B17, IL1RN, CES1, H2AFJ.

Conclusions: We have established two unique in vitro models for the study of enzalutamide and abiraterone acetate resistant CRPC, i.e LNCaP-EnzR and LNCaP-AbiR. These two cell lines presented with a neuroendocrine-like characterizations. These established cell lines could help us gain insight of the mechanism(s) involved in the progression of the prostate cancer and help us develop novel therapeutic method to help our patients.