P062 Transcriptional regulation of RNAs in androgen receptor axis by apigenin compared to cabazitaxel efficiency in prostate cancer cells

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Introduction & Objectives: As a result of microtubule dysfunction, Cabazitaxel (Cbx) exerts its therapeutic activity mainly through cell cycle inhibition in cancer cells. Recent reports have suggested an additional role associated with androgen receptor (AR) for this agent in prostate cancer treatment. Apigenin (Api), another plant-derived phytochemical, has shown promising anticancer activity by regulating several oncogenic signaling pathways. However, its anti-androgenic properties is still unclear. Using AR-positive and androgen-responsive human metastatic prostate cancer cells, LNCaP, we aimed to investigate which agent has more potential to inhibit transcription of AR, PSA, and three AR-targeted/related long non-coding RNAs (lncRNAs) including two oncogenic and one tumor suppressive: Prostate cancer antigen 3 (PCA3), prostate cancer gene expression marker 1 (PCGEM1), growth-arrest-specific transcript 5 (GAS5). Thus, the cell growth inhibitory and possible anti-androgenic properties of Api were firstly compared with the in vitro efficiency of Cbx in the present study.

Materials & Methods: The cells were treated with separately Cbx (0.5-10 nM) and Api (5-80 μM) for 24 h. The individual cell viability inhibition and apoptotic effects of each agent were determined by WST-1 proliferation and Annexin V assays. Then, total RNA extraction was performed from the cells treated with effective concentrations of the agents and expression analysis of the above-mentioned genes were performed using a real-time quantitative reverse transcription polymerase chain reaction (RT-qPCR) system.

Results: Cbx and Api were found to inhibit cell growth in a dose-dependent manner. While exposure of the cells with 5 nM and 10 nM Cbx inhibited cell viability to 56.3% and 46.4%, 40 μM and 80 μM Api reduced cell viability to 55.1% and 48% for 24 h, respectively ($p<0.05$). Based on Annexin V analysis, cell viability reduced to 45.2% and 46.9% at 10 nM Cbx and 80 μM Api treatments. Compared to non-treated control group, the percentage of total apoptotic cells for 24 h were nearly 35.4% and 52.5% at 10 nM Cbx and 80 μM Api, respectively. After treatment with 10 nM Cbx, AR was found to be down-regulated 1.38-fold ($p=0.025$). PSA transcription was not affected by Cbx treatment. However, 80 μM Api reduced both AR and PSA expression by 6.5- and 1.5-fold, respectively ($p<0.001$). PCA3 expression was not altered by either Cbx or Api treatment. Finally, unlike 10 nM Cbx treatment, 80 μM Api significantly increased the GAS5 expression (2.32-fold, $p<0.001$) and decreased the PCGEM1 expression (1.22-fold, $p<0.001$) for 24 h in LNCaP cells.

Conclusions: Taken together, our results show that Api has more potential to induce apoptosis and regulate AR-targeted/related RNA expression levels in metastatic prostate cancer cells compared to Cbx treatment in vitro.