P76 Cand1 in prostate cancer and its implication in therapy resistance to enzalutamide

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Introduction & Objectives: Evidence has accumulated asserting the importance of cullin-RING ubiquitin ligases (CRLs) and their regulator Cullin-associated NEDD8-dissociated protein 1 (Cand1) in various cancer entities. However, the role of Cand1 in prostate cancer (PCa) has not been intensively investigated so far. In the present study, we aimed to assess it the clinical and preclinical setting.

Results: Immunohistochemical analyses of radical prostatectomy specimens of PCa patients showed that Cand1 protein levels are elevated in PCa compared to benign areas. In addition, high Cand1 levels were associated with higher Gleason Scores as well as with higher tumor recurrence and decreased overall survival rates.
In line with clinical findings also in vitro experiments in different PCa cell lines revealed that knockdown of Cand1 reduced cell viability and proliferation and increased apoptosis underlying its role in tumor progression. Using bioinformatics tools, we detected genes coding for proteins linked to mRNA turnover, protein polyubiquitination and proteasomal degradation significantly upregulated in Cand1^{hi} tumors.
Next generation sequencing of PCa cell lines resistant to the anti-androgen enzalutamide showed Cand1 is mutated in enzalutamide-resistant cells, however with little functional and clinical relevant impact in the process of resistance development.

Conclusions: To summarize the present study, we found that high Cand1 levels correlate with PCa aggressiveness.