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**SUN-139**

The development and maintenance of the adult prostate is dependent on the action of androgens, which mediate its effect by binding to the androgen receptor (AR). Dysregulation in the AR signaling axis disrupts transcriptional homeostasis, shifting the balance towards uncontrolled proliferation and driving the progression towards prostate cancer (PCa). The prominent role of AR signaling in prostate carcinogenesis led to the development of androgen deprivation therapy (ADT) as the primary treatment strategy for managing PCa. Despite the success of ADT in early PCa cases, most patients develop resistance to ADT and the cancer ultimately recurs towards a lethal state termed castration-resistant prostate cancer (CRPC). Remarkably, AR signaling is still active in CRPC, suggesting that the progression towards CRPC is still reliant on AR activity. Current treatments are ineffective against CRPC, highlighting the need for alternative therapeutics that can combat the resistant nature of CRPC. To address the need for innovative approaches against CRPC, we used a robust luminescence-based bioassay that can identify novel AR antagonists. We screened plant extracts derived from local fauna by measuring their effect on AR-driven activity using a luciferase-based reporter assay in HeLa cells stably overexpressing hAR (HeLa-hAR). To identify candidate hits, HeLa-hAR cells were treated with DHT to induce AR-dependent luciferase activity, DHT with the AR antagonist bicalutamide as a positive control, and DHT plus the plant extracts. We identified one extract, A32, which showed significant inhibition of AR-dependent luciferase activity without having deleterious effects on cell viability. Secondary validation tests also showed that A32 exhibits a dose-dependent inhibition of AR-driven reporter activity. When testing the effect of A32 on gene expression in LNCaP cells, we observed a down-regulation in the expression of canonical AR target genes such as PSA to degrees similar to bicalutamide. These results suggest that A32 may be an AR antagonist or may target the AR signaling axis. Collectively, this study establishes the use of a luminescence-based reporter assay for the identification of novel AR antagonists from a plant extract library.

# Adrenal

## ADRENAL PHYSIOLOGY AND DISEASE

### *Analysis of ATRX and ZNRF3 Expression and Copy Number Variation in a Pediatric and Adult Cohort with Adrenocortical Tumors*

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**SUN-218**

**Introduction:** Adrenocortical carcinoma (ACC) is a rare malignancy with an incidence of 1 to 2 cases per million/year in adults and with a global survival rate of less than 40% in 5 years. ACC diagnosis was based on Weiss criteria for adult patients. Pediatric patients with adrenocortical tumors (PAT), in general, are associated with better survival in most cases, and the malignant disease is established when local or distant metastases are found. The integrated and extensive genomic-molecular characterization of ACC has resulted in a better understanding of its pathophysiology. Some studies have demonstrated the involvement of *ATRX* and *ZNRF3* genes in adrenal tumorigenesis in pediatric and adult patients with PAT and ACC, respectively. However, these data have not been validated in a Brazilian cohort with a high prevalence of the *TP53* germline R337H mutation. **Objectives:** We aimed to evaluate the *ATRX* and *ZNRF3* expression and copy number variation in a Brazilian cohort of patients with PAT and adults with ACC from a tertiary center. **Patients and Methods:** 34 adults (19 women - 56%) with median age 49 years old (range 18-83) and twelve pediatric patients (7 girls - 58%) with median age three years old (0.8-15 years old) were included in this study. The epidemiological data, clinical presentation, hormonal data, radiological imaging, and genetic background for *TP53* were retrospectively evaluated. MLPA and RT-PCR were employed to evaluate the copy number variation and the gene expression, respectively, of *ATRX* and *ZNRF3* in tumor tissues. **Results:** Adult group: Seven patients out of 27 (25.9%) presented the pathogenic germline mutation pR337H on*TP53*. 20 patients (58.8%) presented metastasis, and 19 (55%) had a fatal outcome. The median global survival was 17.23 months (0.6-185.8 m). Pediatric group: 10 patients (83.3%) presented the pathogenic germline mutation p.R337H on *TP53*. Four patients presented metastasis and only two had a fatal outcome. The median global survival was 42.4months (6.63-125.5m). All tumors were functional. Molecular results: Three out of 33 adult patients (9%), and 2 out of 12 (16.6%) pediatric patients presented deletion on *ATRX*. Four out of 25 adults (16%) and 2 out of 12 pediatric (16.6%) patients showed deletion on *ZNRF3*. There was no correlation between *ATRX* and *ZNRF3* expressions or deletions with the overall survival rate ($p>0.05$). The decrease in the *ATRX* expression was associated with the presence of *TP53* germline mutation in pediatric and adult cohorts (p 0.028). **Conclusion**: We confirmed the presence of alterations on *ATRX* and *ZNRF3* genes in both cohort (adult and pediatric tumors). These results differ from the previous studies, which demonstrated *ATRX* and *ZNRF3* alterations were present in pediatric and adult tumors, respectively. However, prospective studies with larger cohorts are necessary to confirm the prognostic value of *ATRX* and *ZNRF3* genes in PAT and adults with ACC.

# Bone and Mineral Metabolism

## OSTEOPOROSIS AND VITAMIN D

### *Implementation of a High-Risk Fracture Program in an Integrated Healthcare Delivery System*

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