

**Conclusion:**

Elevated ALT can be associated with NAFLD related risk factors. Type 1 diabetics with elevated ALT should be evaluated. And patients with type 1 DM should undergo screening for other autoimmune disease.

**Adrenal****ADRENAL PHYSIOLOGY AND DISEASE*****Investigating the Role of the Liver X Receptor in Potentiating Mitotane Therapy in Adrenocortical Carcinoma***

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**Introduction:** Adrenocortical Carcinoma is a rare aggressive cancer which carries a poor prognosis. Adjuvant mitotane improves survival but is limited by a narrow therapeutic window and severe adverse effects. Liver X receptors (LXRs), part of the nuclear receptor superfamily are highly expressed in adrenal tissue and mediate transcellular and intracellular cholesterol homeostasis. We hypothesise that LXR $\alpha$  inhibition increases toxic lipid accumulation in adrenocortical cancer cells and potentiates the adrenolytic effect of mitotane. **Methodology:** ATCC-H295R and MUC1 ACC cells and were pre-treated with the LXR $\alpha$  inverse agonist SR9243 5 $\mu$ M and antagonist GSK2033 5 $\mu$ M followed by mitotane treatment (20, 40, 50 $\mu$ M) for 6 hours. Cholesterol-methyl- $\beta$ -cyclodextrin treatment was carried out 1hr prior to mitotane. H295R cells were transfected with a LXR $\alpha$  dominant negative construct using lipofectamine. Cell death was assessed using annexin/PI staining and proliferation using MTT assay. Free cholesterol (FC) levels were assayed using filipin staining and lipid droplets via BODIPY<sup>®</sup> and analysed on the Amnis ImageStream<sup>®</sup> imaging cytometer. Downstream targets ABCA1 and ABCG1 were evaluated by qRT-PCR. Lipid droplet associated proteins PLIN 1-4 and hormone sensitive lipase (HSL) expression were evaluated using western blotting. **Results:** Downstream reduction of ABCA1 and ABCG1 expression confirmed LXR $\alpha$  blockade. Mitotane effectively induced dose-dependent H295R apoptotic cell death which was potentiated pharmacologically and genetically by LXR $\alpha$  inhibition. In line with these findings, cholesterol-methyl- $\beta$ -cyclodextrin treatment increased cell death in H295R and MUC1 cells. In addition to inducing cell death, LXR $\alpha$  inhibition decreased proliferation of both cell lines. An increase in FC and a decrease in cholesterol esters was observed

following mitotane treatment in H295R cells. This was accompanied by decreased lipid droplet numbers confirmed by lower expression of lipid droplet associated proteins, PLIN1-3. These effects were potentiated when mitotane was combined with LXR $\alpha$  inhibition. We demonstrate increased HSL activity, which was associated with higher SOAT-1 expression and increasing toxic FC accumulation. Investigation of lipid droplet content BODIPY<sup>®</sup> of both cell lines showed H295R cells preferentially store cholesterol esters and MUC1 cells store triacylglycerides. **Conclusion:** We propose a mechanism for enhancing mitotane's efficacy as an adrenolytic through increased free cholesterol via LXR $\alpha$  inhibition. Targeting the LXR $\alpha$ , its putative ligands, or associated lipid mediators may present a novel therapeutic approach in the setting of primary and metastatic ACC.

**Adrenal****ADRENAL - HYPERTENSION*****Developing a Research Database About Primary Aldosteronism: Rationale and Baseline Characteristics***

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**Introduction** There were limited evidence supporting the management of PA, primarily due to lack of high quality of data. Developing a research database through integrate both retrospective and prospective collected data regarding clinical care and outcomes of patients with PA may provide valuable evidence on management of PA. **Methods** The establishment of PA research database involved two steps. Firstly, patients with confirmation of PA between 1 Jan 2009 to 31 Aug 2019 were identified and data were extracted from EMR. Secondly, patients who have positive confirmatory testing for PA and agree to participate a prospective cohort will be enrolled. Data regarding clinical care and long-term outcomes will be prospectively collected based on the case report forms since 1 Sep 2019. We evaluated the quality of research database through assessment of quality of key variables. **Results** Totally, 904 patients diagnosed as PA in WCH were identified, of which 507 patients had positive confirmatory testing for PA were finally included into the retrospective database. Among included patients, the mean age was 49.2 years old, and the mean BMI was 24.72 kg/m<sup>2</sup>. There were 37 (7.3%) patients diagnosed as chronic kidney disease (CKD), 13 (2.6%) as coronary artery disease (CAD), 95 (18.7%) as diabetes mellitus (DM) and 77 (15.2%) as obstructive sleep apnea-hypopnea syndrome (OSA). The mean systolic blood pressure (SBP) was 155.8 mmHg, and the mean diastolic blood pressure (DBP) was 96.2 mmHg. Among included patients, the lowest serum potassium during admission was 2.96 mmol/L, and the mean serum aldosterone was 26.4 ng/dL. Validation of data extracting and linking showed the accuracy were 100%. Evaluation of missing data showed that the completeness of BMI (95.9%), SBP (1%) and DBP (1%) were high. **Conclusion** Through retrospective and prospective cohort of PA, a research database about PA with high quality and comprehensive data will be established. We anticipate that the research