PhD[2], Paloma Alonso-Magdalena, PhD[1].
[1]Miguel Hernandez University of Elche, Elche, Spain, [2]University of Houston, Houston, TX, USA.

SAT-715

Bisphenol-A (BPA) is one of the highest volume chemicals produced worldwide. It is used as the base compound in the manufacture of polycarbonate plastics, epoxies and resins. Humans are consistently exposed to BPA and consistently it has been detected in the majority of individuals examined. Experimental research in animals, as well as human epidemiological studies, converge to conclude that BPA is a risk factor for the development of type 2 diabetes. In previous studies we have demonstrated that the exposure to BPA during embryonic development promote an increment of pancreatic β-cell mass. This was correlated with increased β-cell division and altered global gene expression in pancreatic β-cells. The aim of this work was to determinate whether ERβ was involved in the in the β-cell mass and proliferation increment observed in male mice offspring. ERβ+/- pregnant mice were treated with vehicle or BPA (10 μg/kg/day) from day 9 to 16 of gestation. Offspring pancreatic β-cell mass was measured at postnatal day 0 (P0) and 30 (P30). For *ex vivo* experiments Wild-type (WT) and ERβ-/- neonates as well as adult male and female mice were used. For *in vitro*, single islets cells were cultured for 48 h in the presence of 10 μmol/L BrdU, and vehicle, BPA (1, 10, 100 nM) or the specific ERβ agonist WAY200070 (1, 10, 100 nM). β-cell proliferation rate was quantified as the percentage of BrdU-positive pancreatic β-cells. *In vivo* exposure to BPA during pregnancy promoted an increment of pancreatic β-cell mass and proliferation in WT mice at P30 which was absent in ERβ -/- mice. In order to explore if these changes were related to a direct action of BPA on pancreatic β-cell division we performed a series of *ex vivo* experiments. Augmented β-cell proliferation rate was observed in BPA-exposed β-cells isolated from both adult male and female WT animals in comparison to controls. The increment was significant at all BPA doses tested. The effect was imitated by the selective ERβ agonist, WAY200070, and was abolished in cells from ERβ-/- mice. We also explored the effects of BPA in pancreatic β-cells from neonates and found an increment in BPA-exposed cells compared to controls, although the difference was only significant at the dose of 1 nM. A similar effect was observed in neonate cells treated with WAY200070 (10 nM). The effects on β-cell replication were abolished in cells from ERβ-/- neonate mice treated either with BPA or WAY200070. Our findings suggest that BPA modulate pancreatic β-cell growth and mass in an ERβ-dependent manner. This could have important implications for metabolic programming of T2DM. Ministerio de Economía y Competitividad, Agencia Estatal de Investigación (AEI) and Fondo Europeo de Desarrollo Regional (FEDER) grants BPU2017-86579-R (AN) and BFU2016-77125-R (IQ); Generalitat Valenciana PROMETEO II/2015/016 (AN). CIBERDEM is an initiative of the Instituto de Salud Carlos III.

Steroid Hormones and Receptors

STEROID BIOLOGY AND ACTION

Characterising the Metabolism, Glucuronidation and Sulfation of C11-oxy C_{19} Steroids

Therina Du Toit, PhD (Biochemistry), Amanda C. Swart, PhD.
Stellenbosch University, Stellenbosch, South Africa.

SAT-742

The metabolism of 11β-hydroxyandrostenedione (11OHA4), a major adrenal C_{19} steroid, was first characterised in our *in vitro* prostate models showing that 11OHA4, catalysed by 11βHSDs, 17βHSDs and 5α-reductases, yields potent androgens, 11keto-testosterone (11KT) and 11keto-dihydrotestosterone (11KDHT) in the 11OHA4-pathway [1]. Findings have since led to the analysis of C11-oxy steroids in PCOS, CAH and 21OHD. However, the only circulating C11-oxy steroids included to date have been 11OHA4, 11keto-androstenedione (11KA4), 11β-hydroxytestosterone (11OHT) and 11KT, with 11KT reported as the only potent androgen produced from 11OHA4. We have identified higher levels of 11KDHT compared to 11KT in prostate cancer tissue and benign prostatic hyperplasia tissue and serum, with data suggesting impeded glucuronidation of the C11-oxy androgens [2,3]. The assessment of 11KDHT and the inactivation/conjugation of the C11-oxy steroids in clinical conditions is therefore crucial.

We investigated the metabolism of testosterone, 11KT, 11OHT, dihydrotestosterone, 11KDHT and 11OHDHT in JEG-3 placenta choriocarcinoma, MCF-7 BUS and T-47D breast cancer cells, focusing on glucuronidation and sulfation. Steroids were assayed at 1 μM and metabolites were quantified using UPC^2-MS/MS. Conjugated steroids were not detected in JEG-3 cells with DHT (0.6 μM remaining) metabolised to 5α-androstane-3α,17β-diol and androsterone (AST), and 11KDHT (0.9 μM remaining) to 11OHAST and 11KAST. 11OHA4 was converted to 11KA4 (12%) and 11KT (2.5%); and 11KT to 11KDHT (14%). In MCF-7 BUS cells, DHT was significantly glucuronidated, whereas 11KDHT was not. 11KAST was the only steroid in the MCF-7 BUS and T-47D cells that was significantly sulfated ($p<0.05$). In parallel we investigated sulfation in the LNCaP prostate model. Comparing sulfated to glucuronidated levels, only DHT was sulfated, 26%. Analysis showed that C_{19} steroids were significantly conjugated (glucuronidated + sulfated) compared to the C11-oxy C_{19} steroids.

As there exists an intricate interplay between steroid production and inactivation, impacting pre- and post-receptor activation, efficient conjugation would limit adverse downstream effects. Our data demonstrates the production and impeded conjugation of active C11-oxy C_{19} steroids, allowing the prolonged presence of androgenic steroids in the cellular microenvironment. Identified for the first time is the 11OHA4-pathway in placenta and breast cancer cells, and the sulfation of 11KAST. Characterising steroidogenic pathways in *in vitro* models paves the direction for *in vivo* studies associated with characterising clinical disorders and disease, which the C11-oxy C_{19} steroids and their intermediates, including inactivated and conjugated end-products, have highlighted.

[1] Bloem, *et al.* JSBMB 2015, 153; [2] Du Toit & Swart. MCE 2018, 461; [3] Du Toit & Swart, JSBMB 2020, 105497.

Bone and Mineral Metabolism

PARATHYROID HORMONE TRANSLATIONAL AND CLINICAL ASPECTS

Dry Cough as Only Sign of a Parathyroid Adenoma Producer of PTH

Antonio Selman-Geara, MD Prof.[1], Antonio Benitez-Camporro, Sonographer, MD[2], Guillermo Defillo-Guerrero, Nuclear Medicine, MD[3], Ammar Ibrahim, Neck Surgeon, MD, FACS[1], Yasmin

Redondo, Cytopathologist, MD[4], L Rodriguez, Pathologist, MD[5], Antoine Selman-Fermin, MD, CCRP[6], Anyel I. Selman-Fermin, Language Services Specialist[1].
[1]Universidad Central del Este, Santo Domingo, Dominican Republic, [2]CRESA, Santo Domingo, Dominican Republic, [3]M. Nuclear, S.R.L., Santo Domingo, Dominican Republic, [4]Laboratorio de Referencia de Anatomia Patologica y Especialidades, Santo Domingo, Dominican Republic, [5]Clinica Dr. Abel Gonzalez, Santo Domingo, Dominican Republic, [6]Children's Hospital of Philadelphia, Philadelphia, PA, USA.

SAT-388

BACKGROUND: The parathyroid adenoma producing an excess of PTH is characterized by hypercalcemia, asthenia, physical weakness and renal lithiasis. **This clinical case is presented only with a dry (non-productive) cough sign of long duration.**CASE: 51-year-old female born in Padre Las Casas, D.R. presenting with **chief complain of dry cough for about four years**. Clinical findings: (03/13/2019) Height 62", Weight 142 lbs, Temperature 36.2 Celsius, BP 90/60 mmHg, RR 16 rpm, HR 60 bpm, on her neck no adenopathies or thyroid changes. Occasional coughing. A **sonographic evaluation of the neck** (04/09/2019) reveals a **solid, heterogeneous nodular image of 0.7 cm x 0.5 cm in the left lobe of the Thyroid** (Fig. 1) which by **FNAB** (04/10/2019) showed a **benign adenomatoid node with cystic changes** (Bethesda II) (Fig. 2). TEST: (03/20/2019) anti-TG 0.10 IU/mL (NV -115), anti-TPO 9.00 IU/mL (NV -34), TG 9.41 (NV -78 ng/mL), TSH 0.34 µIU/mL (VN 0.27-4.20), free T3 2.05 pg/mL (NV 2.04-4.40), **total T3 0.74 ng/mL** (NV 0.83-2.00), total T4 8.46 µg/dL (NV 5.1-14.1), free T4 1.61 ng/dL (NV 0.93-1.71) Calcium 10.4 mg/dL (NV 8.1-10.4), Phosphorus 2.6 mg/dL (NV 2.5-4.5), **PTH-Intact 157 pg/mL** (NV 14.5-87.1) Thyroid-Parathyroid scintigraphy (Sestamibi-Technetium 99mTc04: 15 mCi) (04/23/2019) shows **lower left Parathyroid Adenoma** (Fig. 3). She undergoes surgery (05/23/2019) removing the left thyroid lobe and left inferior parathyroid gland whose pathology shows chronic **nodular colloid goiter**, with areas of **hemorrhage**. **Parathyroid adenoma of main cells** (Fig. 4-5). Post-surgical TEST (06/24/2019) PTH-intact 69.0 pg/mL (NV 14.5-87.1), Calcium 8.6 mg/dL (NV 8.1-10.4), Phosphorus 2.7 mg/dL (NV 2.5-4.5), anti-TG 10.0 IU/mL (NV <115), anti-TPO 9.00 IU/mL (NV <34), TG 8.92 ng/mL (NV <78), **total T3 0.68 ng/mL** (NV 0.83-2.00), **free T3 1.95 pg/mL** (NV 2.04-4.40), total T4 6.40 µg/dL (NV 5.1-14.1), free T4 1.02 ng/dL (NV 0.93-1.71). Post-surgical clinical evaluation (06/21/2019) Weight 142 lbs, Temperature 36.5 Celsius, BP 110/70 mmHg, RR 16 rpm, HR 60 bpm. Patient has not shown signs of coughing. Last TESTS (10/20/2019) Calcium 9.40 mg/dL, Phosphorus 3.10 mg/dL, PTH-intact 24.40 pg/mL, TG 11.90 ng/mL, total T4 6.80 µg/dL, free T4 1.23 ng/dL, total T3 0.88 ng/mL, free T3 2.66 pg/mL, anti-TPO 11.14 IU/mL, anti-TG 10 IU/mL. CONCLUSIONS: Lower left (benign) parathyroid adenoma whose clinical manifestations are not common. Dry (non-productive) cough is not known as a manifestation of elevated PTH-intact. Calcium and Phosphorus levels in normal values. In addition, histological alterations of the left thyroid lobe of benign character with few manifestations of hormonal alterations and normal antibodies. It is of crucial clinical importance to observe and document more cases with similar presentation in order to identify the possible causes of cough with an elevated PTH manifestation.

Healthcare Delivery and Education

EXPANDING CLINICAL CONSIDERATIONS FOR PATIENT TESTING AND CARE

Underdiagnosis of Primary Hyperparathyroidism in the Outpatient Setting of an Academic Health Care System

Nardeen Dawood, BA, MSL[1], Dalena Nguyen, BS[2], Chi-Hong Tseng, BS, MS, PhD[1], Masha Jean Livhits, MD[2], Angela M. Leung, MD, MSc[3], Michael W. Yeh, MD[2].
[1]UCLA David Geffen School of Medicine, Los Angeles, CA, USA, [2]UCLA Section of Endocrine Surgery, Los Angeles, CA, USA, [3]UCLA Division of Endocrinology, Diabetes, and Metabolism, Los Angeles, CA, USA.

MON-123

Background: Primary hyperparathyroidism (PHPT) is the leading cause of hypercalcemia in the outpatient population and is associated with nephrolithiasis, osteoporosis, and further end-organ effects. When indicated, parathyroidectomy is an effective intervention. The aim of this study was to assess the prevalence of patients with hypercalcemia resulting from undiagnosed PHPT within a large, urban, academic healthcare system.

Methods: The study population comprised all patients within UCLA Health. The electronic medical record was queried between 01/01/2016-12/31/2018 to include patients with at least two elevated serum total calcium concentrations (>10.4 mg/dL) within a six-month period in the outpatient setting. Causes of secondary and tertiary PHPT were excluded. In concordance with the PHPT diagnostic criteria outlined by the Fourth International Workshop, we evaluated the proportion of patients with hypercalcemia who were further assessed with a serum intact parathyroid hormone (iPTH) test. The study identified cases of PHPT as defined by confirmed elevated serum total calcium concentrations and elevated or inappropriately normal iPTH concentrations.

Results: There were 7102 patients with a single elevated serum total calcium result who never received a repeat assessment within the study period. Although there were 5617 patients with confirmed hypercalcemia, only 2773 (51%) had an iPTH level assessed within six months of the repeated calcium measurement. Of those who underwent iPTH testing, 1931 (69%) were biochemically confirmed to have classic (34.2%) or normohormonal (35.4%) PHPT; the remaining 31% had an appropriately suppressed iPTH concentration relative to the hypercalcemia.

Conclusions: In a large, academic, tertiary healthcare center, over half of the ambulatory patients with confirmed hypercalcemia did not receive further work-up to assess for possible PHPT. Efforts to improve diagnosis of PHPT and expand curative treatment have the potential to decrease