

of thyroid papillary carcinoma is generally characterized by slow progression and minimal invasion. Although the TPMC subtype usually has good prognosis, its early recognition has clinical relevance because it may present with regional lymph node metastasis, as well as increased risk of recurrence. **AIM OF THE STUDY:** The aim of the study is to identify the epidemiologic profile of the population diagnosed with TPMC, as well as the signs and symptoms observed in these patients. This study intends to guide early clinical suspicion of thyroid tumors; in order to propose assertive forms of management and prevention of undesirable outcomes. **PATIENTS AND METHODS:** Retrospective cohort study based on medical records of patients diagnosed with TPMC at University Hospital of Brasilia-Brasil, from 1999 to 2017. The clinical aspects analysed were: gender; race; age of the patient when the diagnosis was made; symptoms reported by the patients regarding the pathology and comorbidities. **RESULTS:** Fifty-eight patients who underwent thyroidectomy for variable thyroid criteria were included in this study. 87,93% were women, (seven fold higher female prevalence of the TPMC). Mean age of diagnosis was 42, $94 \pm 11,4$. Regarding the race, the majority of the patients had self-entitled as mixed race, which corresponds to 39,65% of the sample. Symptoms reported included dysphagia (29,31%), dyspnea (17,24%) and feeling of neck compression (13,79%). Even though these aspects of the clinical approach are significant diagnosis tools, only 26,5% of the patients in this sample attested those kinds of signs/symptoms. Considering that actual clinical manifestation is relatively rare, total inclusion of the anatomic specimen is useful in this unsettling scenarios. Among the most commonly reported comorbidities, benign thyroid affections were the most prominent, such as multinodular goiter and hypothyroidism. **CONCLUSION:** Analysis of the data endorses that the TPMC does not have a well defined clinic presentation. Nonetheless, dysphagia is the most reported symptom. Analysis of the data pointed to a higher prevalence of the pathology in women in their 40s, which can be used as parameter of investigation on patients that have symptoms that cannot be explained by other pathologies. Although TPMC usually presents with good prognosis, the non incidental groups may present with aggressive behavior and should be treated as papillary thyroid carcinoma. Despite that, fine needle aspiration and ultrasonography are the preferable methods in the evaluation of thyroid tumors.

Steroid Hormones and Receptors

STEROID BIOLOGY AND ACTION

Advantages and Limitations of an Integrative Measurement for All Serum Androgens and Anti-Androgens

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Abstract:

Background: Analytic measurements of a hormone in bodily fluids are a cornerstone of clinical evaluation. However,

clinical presentation may be affected also by currently unmeasured modulators of hormonal function. An alternative could be to measure the cumulative effect of all factors present in a bodily fluid on the function of a hormone receptor. Prior studies showed an androgen receptor (AR) BioAssay to accurately measure urine androgens in males undergoing testosterone (T) supplementation (1). The factors integrated by the AR BioAssay include androgens, anti-androgens and, in serum, androgen binding proteins affecting ligand availability.

Methods: The AR BioAssay was exposed to male and female serum samples obtained from the CDC's Hormone Standardization (HoSt) Program, and to female serum samples from the UCSF PCOS Tissue Bank registry. AR activity was quantified against a testosterone standard curve and recorded as 'T-equivalent' ('T-eq') androgen activity units.

Results: In 40 CDC HoSt sera added directly (no extraction) to AR BioAssay cells, androgen activities ranged from 2.57 to 298 ng 'T-eq'/dl. In the 20 'male' CDC HoSt sera (T>150 ng/dl), the androgen activity measurements were uniformly less (0.35 ± 0.10) that of the T-measurement. By contrast, in the 20 'female' CDC HoSt sera, in which T concentrations are typically lower than the affinity of T for sex hormone binding globulins such that more of the T is available to the AR BioAssay, the measured androgen levels were on average 1.45-fold higher than the T concentration. This androgen to T comparison showed high variability in females with 5 of 20 CDC HoSt samples having androgen concentrations more than double that of T (maximum, 6.1-fold). In female serum samples from the PCOS registry, androgens were higher in patients with a PCOS diagnosis (57.7 ± 17.6 ng 'T-eq'/dl; n = 23) compared to women not meeting formal PCOS criteria (38.1 ± 10.8 ng 'T-eq'/dl; n = 4); androgen values again averaged 1.40-fold (maximum, 4.9-fold) that of the T measurements, regardless of PCOS diagnosis.

Conclusions: Androgen-binding globulins appear to most influence androgen activity levels in male serum. In females, the lower T concentrations may minimize the impact of androgen-binding proteins and permit the impact of non-T androgens to be more pronounced with possible clinical consequence. Further investigations are needed to determine whether functional androgen measurements may improve clinical diagnosis of certain conditions.

Reference: (1) Bailey et al (2016) PLoS One 11(3):e0151860

Genetics and Development (including Gene Regulation)

ENDOCRINE DISRUPTING CHEMICALS

Structure-Based Discovery of Hydraulic Fracturing Chemicals as Novel Androgen Receptor Antagonists

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SAT-722

Hydraulic fracturing (HF) technology is increasingly utilized for oil and gas extraction operations. The widespread use of

HF has led to concerns of potential negative impacts on both the environment and human health. Indeed, the potential endocrine disrupting impacts of HF chemicals is one such knowledge gap. Herein, we used structure-based molecular docking to assess the binding affinities of 60 HF chemicals used in California to the human androgen receptor (AR). Five HF chemicals had relatively high AR binding affinity, suggesting the potential to disrupt AR effects. We next assessed androgenic and antiandrogenic activities of these chemicals *in vitro*. Of the five candidate AR ligands, only Genapol[®] X-100 was found to significantly reduce the AR transactivation by 22%. To better understand the structural effect of Genapol[®] X-100 on the potency of receptor inhibition, we compared the antiandrogenic activity of Genapol[®] X-100 with that of its structurally similar chemical, Genapol[®] X-080. Interestingly, both Genapol[®] X-100 and Genapol[®] X-080 elicited a significant antagonistic effect with 20% relative inhibitory concentrations (RIC₂₀) of 0.43 and 0.89 μ M, respectively. This indicated that Genapol[®] X-100 was more potent in inhibiting AR than Genapol[®] X-080, consistent with longer Genapol[®] X-100 chain length causing greater potency of AR activity inhibition. Furthermore, we investigated the mechanism of AR inhibition of these two chemicals *in vitro*. The result revealed that both Genapol[®] X-100 and Genapol[®] X-080 inhibited AR through noncompetitive binding mechanism. The effects of these two chemicals on the expression of AR responsive genes such as *PSA*, *KLK2*, and *AR* were also investigated. Genapol[®] X-100 and Genapol[®] X-080 notably altered the expression of these genes at relatively low concentrations of 0.5 μ M to 1 μ M. Using these integrated *in vitro* and *in silico* approaches, we identified HF chemicals as novel noncompetitive AR antagonists. Our findings heighten awareness of endocrine disruption by HF chemicals and provide evidence that noncompetitive antiandrogenic Genapol[®] X-100 could possibly cause adverse endocrine health effects in humans.

Genetics and Development (including Gene Regulation)

G PROTEIN-COUPLED RECEPTOR SIGNALING IN ENDOCRINE SYSTEMS: NOVEL MECHANISMS IN HEALTH AND DISEASE

Fetal Sex Impacts First Trimester Maternal-Fetal Communication in Humans

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OR24-07

The placenta serves as a regulator of fetal growth throughout pregnancy. Signaling at the maternal-fetal interface is critical

during placentation and lays the groundwork for placenta function, affecting pregnancy outcomes. Fetal growth is impacted by fetal sex, with males larger than females, and maternal gestational diabetes and obesity independently increase the risk of macrosomia in male fetuses only. We previously demonstrated differentially expressed genes (DEGs) among sexes involves ancient canonical pathways and metabolic functions in placenta tissue. As these are likely impacted by signaling at the maternal-fetal interface, our aim here was to identify sex differences in signaling at the maternal-fetal interface and among individual cell types within the placenta to explain these differences. RNA-sequencing of first trimester placenta and maternal decidua as well as single cell RNA-sequencing in first trimester placenta was performed in ongoing pregnancies. We identified 91 sexually dimorphic receptor-ligand pairs across the maternal-fetal interface. From these, 35 of 115 receptors and/or ligand genes were also found to be upstream regulators of pathways critical in sexually dimorphic placentation which may define regulation. Single cell analysis identified five major cell types (trophoblasts, stromal cells, hofbauer cells, antigen presenting cells, and endothelial cells), and all had sexually dimorphic genes. Among individual cell types, ligands from the CC-family of cytokines were most highly representative in females, with their corresponding receptors present on the maternal surface. Furthermore, upstream regulator analysis of sexually dimorphic genes demonstrated TGF β 1 and estradiol to significantly affect all cell types. Dihydrotestosterone, which is produced by the male fetus, was an upstream regulator that was most significant for the trophoblast population. In addition, gene ontology enrichment analysis identified distinctive enriched functions between male and female trophoblasts, with cytokine mediated signaling pathways most representative. *MUC15* and *NOTUM* were the most highly expressed sexually dimorphic autosomal genes found in distinct cell types of the trophoblast population, cell types critical for placentation and nutrient exchange. Thus, differences in hormone and immune signaling pathways may account for differential gene expression and differences in trophoblast function during placentation, which may in turn explain developmental differences, including fetal size, well-being, and overall outcomes.

Adrenal

ADRENAL - HYPERTENSION

Comparison of the Seated and Recumbent Saline Infusion Test for the Diagnosis of Primary Aldosteronism in Chinese Population

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MON-192

Abstract

Background:

None of the diagnostic tests for primary aldosteronism (PA) are ideal according to the current literature. In a