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 ($RIC_{20}$) of 0.43 and 0.89 μM, 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 μM to 1 μM. 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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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 TGFβ1 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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Abstract

Background:

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