signaling pathways that are involved in turmorigenesis and proliferation. We isolated EVs from the conditioned media of human wild-type hPheo1 cells and hPheo1 cells with shRNA *SDHB* knockdown. The EVs from three separate preparations of each group were characterized by nanoparticle tracking analysis, transmission electron microscopy, and Western blotting using antibodies against different types of EV and one non-EV marker. Our results show small EVs from the *SDHB* knockdown hPheo1 cells increased the activation of phosphotyrosine residues in wild-type cells compared to cells treated with control EVs from the same cell type. Additionally, our data show these EVs increase phospho-STAT3 compared to the control EVs (3843.10 +/- 1138.89 vs. 213.65+/- 40.75; p<0.05; n=3) in cultured wild-type hPheo1 cells. Protein tyrosine kinases (PTKs) control various cellular processes including growth, differentiation, and metabolism by activating various signaling pathways including STAT3. The significance of these findings is that in some cancers, elevated succinate from a *SDHx* mutation has been shown to activate STAT3 which may explain a possible pathway for tumorigenesis. Studies from other investigators have shown that STAT3 expression is elevated in malignant PPGL tissues. Through enriched EV analysis our findings have confirmed the role of STAT3 in *SDHB* deficient cells. Additional studies are needed to identify other metabolites that are enriched in EVs that regulate phosphorylation of tyrosine residues and STAT3 activation.

Adrenal

ADRENAL - BASIC AND TRANSLATIONAL ASPECTS

Human Adrenal Cortical Zone Changes With Aging

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Background: Previous adrenal morphological studies have shown that the zona reticularis (ZR) and the zona glomerulosa (ZG) decrease in size with aging. Although several lines of evidence indicate that the hypothalamic-pituitary-adrenal axis becomes hyperactive in elderly, little is known about age-related transformations of the adrenal zona fasciculata (ZF). **Objectives:** To investigate the morphological and functional changes of the adrenal cortex across the adult life span, with emphasis on: 1) the understudied ZF, and 2) potential sexual dimorphisms. **Methods:** We used immunohistochemistry to evaluate the expression of several cortical proteins: aldosterone synthase (CYP11B2), visinin-like protein 1 (VSNL1), 3β-hydroxysteroid dehydrogenase type II (HSD3B2), 11β-hydroxylase (CYP11B1) and cytochrome b_5 type A (CYB5A). The ZF area was estimated by subtracting the VSNL1-positive (a ZG marker) area from the HSD3B2-expressing area (ZG and ZF). All captured images were quantitated by ImageJ. In addition, we employed liquid chromatography-tandem mass spectrometry to quantify the morning serum concentrations of 6 steroids: cortisol, 11-deoxycortisol (11dF), 17α-hydroxyprogesterone (17OHP4), 11-deoxycorticosterone (DOC), corticosterone, and androstenedione (A4). The Mann-Whitney *U* test and Spearman's rank correlation coefficients were used for statistical analysis, as appropriate. **Results:** We included 60 adrenal glands from 30 men and 30 women, with ages between 18–86 years. The total cortical area was positively correlated with age (r=0.34, p=0.008), and this association was significant only in men (p=0.02). Both the total (VSNL1-positive) and functional ZG (CYP11B2-positive) areas declined abruptly with aging in men (r=-0.57 and -0.76, p=0.001 and p<0.0001, respectively), but not women (p=0.06 and 0.27, respectively). The CYB5A-positive area, marking the ZR, correlated negatively with age (r=-0.76, p<0.0001) in both sexes. In contrast, the estimated ZF area showed a strong positive correlation with age both in men (r=0.59, p=0.0006) and women (r=0.49, p=0.007), while CYP11B1-positive area remained stable across ages (p=0.86). Finally, we measured morning levels of 6 steroids in 149 men and 149 women, with ages between 21–95 years, matched for age and body mass index. Serum cortisol, corticosterone, and DOC levels remained relatively stable across ages (p=0.38, 0.64 and 0.25, respectively), while 11dF levels increased slightly with age (r=0.16 and p=0.007), particularly so in men (p=0.005). Expectedly, 17OHP4 and A4 declined with aging (r=-0.37 and -0.37, p<0.0001 for both). **Conclusions:** In contrast with the ZG and ZR, the ZF and the total adrenal cortex area enlarge with aging. An abrupt decline of the ZG occurs with age in men, but not in women, possibly contributing to sexual dimorphism in cardiovascular risk.

Adrenal

ADRENAL - BASIC AND TRANSLATIONAL ASPECTS

Intracellular Cholesterol Metabolism in Aldosterone-Producing Adenoma.~A Possible Association With Cellular Morphometry and Genotype~

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Introduction: Primary aldosteronism (PA) is the most common cause of secondary hypertension. More than 70% of APAs have been reported to have KCNJ5 somatic mutation in Asian countiries. Patients with KCNJ5 mutated APAs generally harbor high plasma aldosterone concentration (PAC), and are mainly composed of clear tumor cells containing abundant lipid droplets. However, an association among intracellular cholesterol metabolism, morphological features and genotypes in tumor cells has