of the metabolic syndrome (MetS) (2). These effects are thought to be mediated by the glucocorticoid receptor, a nuclear receptor showing affinity for both glucocorticoids and mineralocorticoids. In this study, we examined plasma concentrations of cortisol and aldosterone, corticosterone and 11-deoxycorticosterone were analyzed by electrospray ionization-liquid chromatography-tandem mass spectrometry (ESI-LC-MS/MS). Metabolic parameters were assessed to establish the presence of the MetS using NCEP-III criteria. Subcutaneous and visceral adipocyte cell size was measured by histomorphometry.

**Results:** We found HDL-triglycerides to be positively associated with levels of 11-deoxycorticosterone, 11-deoxycortisol, corticosterone, cortisol, androstenedione and cortisol (p<0.05 for all). 11-deoxycorticosterone concentration was also negatively associated with waist circumference (-0.294, p<0.05), LDL-cholesterol and LDL-triglyceride content (-0.264 and -0.362, p<0.05) whereas cortisol level was positively associated with fasting glucose (0.3, p<0.05). Our model including mineralocorticoids predicted systolic blood pressure (R²=0.303), while the one including glucocorticoids predicted HDL-cholesterol (R²=0.495). In addition, as expected, we found that women with the MetS were characterized by significantly higher percentage body fat and displayed subcutaneous and visceral adipocyte hypertrophy (p<0.05). Interestingly, women with the MetS also showed a trend for lower plasma cortisol concentrations (p=0.07).

**Conclusion:** Our data suggest that glucocorticoids and mineralocorticoids are associated with individual components of the MetS in women.

1. Tchernof et al. (2013), Physiol Rev, 93(1);
2. Constantinopoulos et al., (2015), Eur J Endocrinol, 172(1)

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**Tumor Biology**

**NOVEL REGULATORS OF BREAST CANCER PROGRESSION**

**Small Heterodimer Partner Modulates Antigen Presenting Myeloid Cells to Impair Regulatory T Cell Expansion, Promoting Anti-Tumor Immunity in Models of Breast Cancer:**

Sayyed Hamed Shaboei, BS², Adam T. Nelson, BS², Madeline A. Henn, BS², Ashley E. Mathews, n/a², Joy J. Chen, n/a², Varsha Vembar, n/a², Anna Vardanyan, BS², Liqian Ma, Master of Science², Yu Wang, MS¹, Lionel Apetoh, PhD², Erich Russell Nelson, BSc,PHD².

¹University of Illinois at Urbana-Champaign, Urbana, IL, USA, ²University of Illinois at Urbana Champaign, Urbana, IL, USA, ³INSERM, Dijon, France.

**OR05-01**

Immune checkpoint blockade has had underwhelming responses in breast cancer, in part due to the highly immune suppressive microenvironment. As a result, breast cancer continues to be the second most common cancer-related mortality amongst women, providing strong rationale for the development of new therapeutic approaches. Elevated circulating cholesterol is a poor prognostic, while breast cancer patients taking cholesterol-lowering drugs display increased time to recurrence. We and others have previously demonstrated that cholesterol metabolites mediate these effects by promoting breast cancer growth and metastasis, in part by suppressing the immune system. Therefore, given the demonstrated importance of cholesterol and its metabolites in breast cancer pathophysiology and immunology, we hypothesized that proteins involved in the regulation of cholesterol homeostasis would influence cancer progression. Through informatics analysis of breast tumors, we found that elevated expression of Small Heterodimer Partner (SHP; NR0B2) was a favorable prognostic. Antigen presenting cells such as macrophages and dendritic cells were found to express SHP, and manipulation of SHP altered the expression of genes involved in cross-talk with T cells. Intriguingly, when activated T cells were co-cultured with macrophages overexpressing SHP, there was a decrease in the expansion of regulatory T cells (Tregs) and vice versa in the absence of SHP. Adoptive transfer studies confirmed that loss of SHP resulted in immune suppressive Tregs. We hypothesized that myeloid cell-expressed SHP would promote immune surveillance and tumor clearance. In support of this hypothesis, tumors in the MMTV-PyMT model of mammary cancer grew at an accelerated rate in SHP-knockout mice. Tumors from these mice had significantly more Tregs and fewer effector T cells. Furthermore, orthotopic mammary tumor grafts grew at an increased rate in mice lacking SHP expression in myeloid cells (SHPfl/fl;LysMCre), compared to controls. A small molecule agonist of SHP impaired primary and metastatic tumor growth, and significantly enhanced the efficacy of immune checkpoint blockade in murine models of mammary cancer. Therefore, SHP represents a potential target to decrease suppressive Tregs, thereby allowing for immune-clearance of tumors.

**Neuroendocrinology and Pituitary**

**CASE REPORTS IN SECRETORY PITUITARY PATHOLOGIES, THEIR TREATMENTS AND OUTCOMES**

**Surprising Transformation of a Microprolactinoma to a Macroprolactinoma**

Diana Athonevarangkul, MD,PhD¹, Hillary Wyeth Hosier, MD¹, Brian Wojcicki, MD¹, Silvio E. Inzucchi, MD¹.

¹Yale New Haven Hospital, New Haven, CT, USA, ²Yale School of Medicine, Stratford, CT, USA.

**SAT-258**

**Background:** Microprolactinomas are typically benign tumors that rarely become macroprolactinomas. We present a rare case of a microprolactinoma that, after discontinuation of dopamine agonist (DA) therapy, transformed into a macroprolactinoma over a period of 6 years. **Clinical Case:** A 16-year-old woman initially presented for evaluation of galactorrhea without menstrual irregularities and was found to have elevated prolactin (68 ng/ml, normal range: 0-20), and a 4 mm pituitary microadenoma on MRI imaging.

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The patient was otherwise asymptomatic and other pituitary hormone levels were normal. She was treated with DA therapy (cabergoline 0.50 mg/week) which normalized her PRL level and improved but did not completely resolve the galactorrhea. She was then lost to follow up for 6 years. During that time, she discontinued cabergoline, but was still able to conceive, delivering a healthy baby after 2 years and breastfed briefly. She re-presented to her gynecologist 4 years after delivery for galactorrhea and secondary amenorrhea, both persistent since childbirth. Re-evaluation at that time revealed a much higher PRL level (432 ng/mL) and significant interval growth of the previous microadenoma to a 2.6 cm macroadenoma, now with extension into the left cavernous sinus, suprasellar cistern, with mass effect on the optic chiasm. The patient was retreated with cabergoline up to 3 mg/week, with a near-normal PRL level being achieved at 9 months (28 ng/mL). Repeat MRI revealed modest decrease of the adenoma to 2.4 cm. Galactorrhea resolved with reduction in PRL. However, amenorrhea persisted. Estradiol (30 pg/mL, 19-357 pg/mL) was low normal with normal withdrawal bleeding to medroxyprogesterone (MPA) challenge indicating reasonable estrogenization. She was treated with MPA to achieve regular cyclic bleeding every 3 months. Conclusion: This is an unusual case demonstrating significant growth of a microprolactinoma, which is typically a stable/indolent neoplasm, to a macroadenomatosis with invasive features. Previous studies of untreated microprolactinomas have shown that they undergo only subtle to minimal growth over 3 to 6 years and none transformed to a macroadenomatosis despite significant rises in PRL levels. In this clinical case, given the 6 intervening years that had elapsed in between MRIs, we cannot determine whether this represented moderate, progressive growth during that period after the discontinuation of DA therapy or whether the tumor had grown during pregnancy with its known stimulatory effects from hyperestrogenemia. The patient will require close follow-up to ensure ongoing shrinkage or at least stability of the adenoma and ongoing control of her hyperprolactinemia.

References: 1. Fertility and sterility 39, 753-760 (1983). 2. Dietemann, J.L, et al. Neuroradiology 25, 133-138 (1983). 3. Garcia, M.M et al. Journal of endocrinological investigation 18, 450-455 (1995).

**Thyroid**

**HPT-Axis AND THYROID HORMONE ACTION**

**Chronic Stress During Adolescence of Rats Shows Sex Dimorphism in the Thyroid Axis Response to Voluntary Exercise in Adulthood**

Marco Antonio Parra-Montes de Oca, MSc, Angélica Gutiérrez-Mata, BS, Jean-Louis Charli, DSc, Patricia Joseph-Bravo, PhD.

Instituto de Biotecnología, UNAM, Cuernavaca, Mexico.

SAT-451

Exposure to chronic stress during adolescence causes long-term effects on the response of Hypothalamus-Pituitary-Adrenal (HPA) axis, affecting behavior and energy homeostasis. Voluntary exercise activates the HPT-Thyroid (HPT) axis allowing efficient fluxes of substrates to active target organs. Chronic stress in adult rats blunts HPT axis response to voluntary exercise in a sex-dependent manner (Front Endocrinol 10(418):1-13, 2019). As adolescents show sex-dependent responses to stress, we sought to evaluate the effect of chronic stress at this period in the response of HPT axis to voluntary exercise in adulthood. Wistar male and female rats were divided in an undisturbed group (Control, C) and one group exposed to chronic variable stress (CVS) where the rats were daily subjected to different stressors during postnatal day (PND) 30 to 60 for females and PND 30 to 70 for males. At adulthood (PND 74 for females and PND 84 for males) rats were exposed to running wheel following published protocol (Endocrinology 155:2020-2030, 2014). As females are more susceptible to stress during adolescence than males, additional independent experiments were performed with female rats kept in group or individual housing, since PND 30 (2 per cage or isolated (Iso)). At PND 64, Iso rats were housed in pairs and exposed to CVS every 3 days until PND 80; later, rats were exercised 26 days. Hormones were quantified by ELISA or RIA; mRNA expression was determined by RT-PCR. Voluntary exercise reduced fat mass in C groups, dependent on the amount of exercise performed; stressed rats exercised did not lose fat, indicating that adolescent stress avoids an appropriate energy distribution during exercise. The expression of Crh and Aqp in hypothalamic paraventricular nucleus (PVN) decreased in stressed groups mainly in females, as reported. Exercise decreased corticosterone levels only in C rats, suggesting that CVS during adolescence modifies the HPA axis response to exercise. CVS inhibited Pome expression induced by exercise and increased Npy expression in arcuate nucleus, decreased Trh expression in PVN for both sexes and in dorsomedial hypothalamus in males. Thyroid hormones were not altered in CVS males and Iso females; however, T3 and T4 levels were high in CVS females, so different stress exposures may modify the HPT axis state in females. The response to exercise of the target organs of thyroid hormones reveals with more accuracy the activity of HPT axis, exercise stimulated the expression of Adrb3 and Dio2 in brown adipose tissue of C females, and the expression of Dio2 and Pgc1a in skeletal muscle (gastrocnemius) of both sexes, changes attenuated by CVS. These results indicate that chronic stress during adolescence blunts the response of HPT axis to voluntary exercise, strongly in females than males.

**Adipose Tissue, Appetite, and Obesity MECHANISMS AND TREATMENT OF OBESITY IN HUMANS**

**Congenital Leptin Deficiency: Clinical Insights from the First Reported US Cases**

Laura C. Torchen, MD1, Beth Hakamy, MBBS2, Leo I. Gordon, MD3, Erica E. Marsh, MD MSCF3, Nabeel R. Yaseen, MD, PhD4, Lisa M. Neff, MD, MS5.

1Northwestern University, Chicago, IL, USA, 2University of Michigan, Ann Arbor, MI, USA.

**OR33-03**

**Background:** Congenital leptin deficiency (CLD) is a rare autosomal recessive form of monogenic obesity caused by loss-of-function mutations in the leptin gene. Targeted therapy is available in the form of recombinant human