results suggest a mechanism where near-UV sensitive hypothalamic OPN5 neurons regulate BAT thermogenesis directly, proposing that the mammalian autonomic thermoregulatory apparatus is light responsive.

**Adrenal**

**ADRENAL - TUMORS**

**Distinct Vitamin D Receptor DNA Methylation Profiles Are Associated With the Outcome of Pediatric Patients With Adrenocortical Tumors**

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SAT-LB36

Pediatric adrenocortical tumors (pACT) are rare, display complex genomic background and lack robust prognostic markers. Very recently, distinct genomic methylation profiles of pACT were associated with prognosis. The vitamin D receptor (VDR) was shown to be underexpressed in ACT, especially in carcinomas (ACC). In adult ACC, VDR inactivation by methylation was demonstrated. On the other hand, VDR activation was shown to inhibit ACC proliferation in vitro and in vivo.

**Aim:** To evaluate VDR DNA methylation profile and its clinical and prognostic significance in pediatric ACT.

**Methods:** Genomic DNA methylation from 57 pACTs [40 girls; median age: 2.1 (0.2-16.4) years] was assessed using Infinium Methylation EPIC BeadChip Array. Unsupervised hierarchical clustering analysis (Ward method, R Stats Package) was performed considering the M-values of the 49 probes targeting the whole extension of VDR gene contained in the array. Clinical, histopathological and molecular features, as well as pACT VDR mRNA levels (qPCR) and nuclear immunoreactivity (IHC) were used for association analysis.

**Results:** Hierarchical clustering identified three clusters of pACT. Methylated VDR-targeted probes (M-values different from 0; n=37) composed the VDR methylation profile, which differed significantly between the clusters [M-values: C1=1.77 (1.1-1.9) (low), C2=2.15 (1.7-2.7) (intermediate), and C3=2.65 (2.2-3.1) (high); p<0.0001]. The C1 cluster comprised a set of patients with favorable outcome (n=18), who were younger (p=0.035), did not present metastasis at diagnosis (IPACTR stage IV) or after surgery, nor were diagnosed with carcinomas (Wieneke criteria ≥4), were not carriers of somatic Beta-catenin activating mutations, or died. Although cluster C2 patients (n=21) presented intermediary disease features, only 2 patients died and the overall outcome was positive. Instead, the C3 cluster concentrated patients (n=18) with non-localized/metastatic disease (IPACTR stages I/II vs. III/IV; p=0.004), post-surgical metastasis/recurrence (p=0.009), and patients who needed adjuvant chemotherapy (p=0.005). Moreover, C3 patients had lower overall and disease-free survival rates (log-rank: p=0.001 and p=0.014, respectively). VDR methylation was not associated with sex, clinical presentation, P53 mutations, nor with tumor VDR mRNA expression or nuclear immunoreactivity.

**Conclusions:** Three VDR methylation profiles were associated with distinct pACT clinical features and outcome. High VDR methylation was associated with worst outcome. Fully functioning VDR may play a beneficial role against pediatric adrenocortical tumorigenesis. This finding highlights the potential of targeting VDR as an adjuvant therapeutic target.

**Reproductive Endocrinology**

**FEMALE REPRODUCTION: BASIC MECHANISMS**

**Clinical Case Series of Augmented Fertility in Females After Administration of an Amino Acid Blend That Enhances Release of Human Growth Hormone**

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MON-LB003

Supplementation with adjuvant therapies, including growth hormone (hGH), is commonly used to improve fertility treatment outcomes. hGH is important for normal female fertility; low hGH has been associated with causes of infertility and impaired fertility, including polycystic ovarian syndrome (PCOS), endometriosis, diminished ovarian reserve (DOR), and advanced maternal age. A novel, low dose, orally administered amino acid blend has been previously shown in a double-blind, randomized, placebo-controlled, crossover clinical trial to produce a statistically significant increase in endogenous hGH secretion. In this clinical case series, we report outcomes in 7 women with infertility or impaired fertility and conditions associated with low hGH who administered the amino acid blend during fertility treatment (n=5) or timed intercourse/spontaneous pregnancy (n=2). Medical history included conditions associated with impaired fertility and low hGH: endometriosis (n=3), PCOS (n=2), and poor response to ovarian stimulation/history of failed in vitro fertilization (IVF) (n=3). The amino acid blend (containing 2.9 g of L-lysine, L-arginine, oxo-proline, N-acetyl-L-cysteine, L-glutamine, and schizonepeta) was administered daily on an empty stomach. Outcomes included embryo quality and success of embryo transfer (for IVF) and successful pregnancy/live births. Mean±SD age was 33±5 years (range 27-38) and BMI was 27±7 kg/m² (range 21-37). Time to pregnancy ranged from 1 week to 9 months (median 3 months) prior to egg retrieval for IVF (n=4),
intrauterine insemination (n=1), or timed intercourse/spontaneous pregnancy (n=2). For women with a history of failed IVF (n=3), there was an improvement in oocyte retrieval, a higher fertilization rate, and a greater number of high-quality embryos compared to previous IVF attempts. There were 2 twin pregnancies (both following IVF). All 7 pregnancies resulted in live births. Consistent with previous studies, the amino acid blend was well tolerated; no adverse events were observed. We report a case series of successful pregnancy in 7 women with conditions associated with low hGH including PCOS, endometriosis, and poor response to ovarian stimulation/history of failed IVF who administered the amino acid blend concomitant with fertility treatment or who reported spontaneous pregnancy. This may represent a potential low-risk and cost-effective treatment to improve IVF success and increase pregnancy rates in individuals with infertility or impaired fertility.

Neuroendocrinology and Pituitary CASE REPORTS IN SECRETORY PITUITARY PATHOLOGIES, THEIR TREATMENTS AND OUTCOMES

A Case of Central Hyperthyroidism From a TSH Secreting Pituitary Adenoma
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SAT-LB55
This is a case of a 41 year old Filipino female, with one month history of palpitations, unintentional weight loss and increased frequency of bowel movement. Patient was tachycardic and had a slightly enlarged thyroid on physical exam. There were no cushingoid or acromegalic features. Initial work-up revealed elevated TSH 7.10 U/mL prompting referral to an endocrinologist who had an initial consideration of central hyperthyroidism, MRI was done revealing a pituitary adenoma with dimensions of 7.4 x 11 x 5.8 mm. Prolactin level was at 118.9 ng/mL, gonadotropins (FSH 5 mIU/mL, LH 4.3 IU/L) were within normal range for pre-menopausal non pregnant women and early 24h urine cortisol was within normal at 63.79 nmol/day. Patient was started on propranolol 40 mg thrice daily and methimazole 20 mg twice a day which prompted slight relief. She was also referred to neurosurgery service for further management. Patient underwent transsphenoidal surgery which was tolerated well. Subsequent clinical course revealed improvement of hyperthyroid symptoms with no evidence of post-operative complications such as hematomas, CSF leak, vision loss, diabetes insipidus or central adrenal insufficiency. Immunohistochemical staining was positive for TSH.

On outpatient follow-up, repeat thyroid function tests were within normal with TSH 1.260 and free T4 15.07 pmol/L. Patient is currently symptom free and off methimazole or propranolol. Future plans include a repeat MRI after 6 months of surgery and hormonal testing to confirm cure.

Genetics and Development (including Gene Regulation)

GENETICS AND DEVELOPMENT AND NON-STEROID HORMONE SIGNALING II

A Pilot Genome Wide Association Study (GWAS) on Primary Aldosteronism Patients in a Multi-Ethnic Malaysian Cohort
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MON-LB129
Abstract: Studies on excised aldosterone-producing lesions have found somatic mutations in five genes (KCNJ5, CACNA1D, ATP1A1, ATP2B3, and CTNNB1) commonly causes the excess aldosterone production. Interestingly, Oriental cohorts had the highest frequency of KCNJ5 mutations whereas CACNA1D mutations were most common in Black African Caribbean patients, suggesting that genetic background affects the prevalence and distribution of aldosterone-driving somatic mutation. We therefore aimed to identify the common germline variants that associates with excess aldosterone production through performing a pilot genome wide association study (GWAS) on primary aldosteronism (PA) patients. GWAS was performed using the Human Infinium OmniExpressExome-8 v1.4 BeadChip containing 960,919 markers to compare gDNA of 154 PA patients with 78 healthy controls. Samples were checked for sex discordance, heterozygosity rate, missing rate and the degree of recent shared ancestry for each pair of individuals using the PLINK program and Genome Studio (Illumina). In total, 150 patients and 75 controls (112 males and 113 females) were included in the downstream analysis. 630,749 markers that passed quality control steps (missing call rate <95% and minor allele frequency in controls >1%) were used to perform association analysis using the Chi-square Test which was then subjected to multiple testing corrections (Bonferroni correction). As expected with a pilot sample size, no variants passed the suggestive significant threshold of Bonferroni corrected P-value < 5 x 10^-6 (-log10 P = 5.3). However, 27 SNPs had the uncorrected P-value<0.0002, odds ratio >2, and differences of frequencies in cases compared to control >0.1 or < -0.2, of which 3 genes (SRGAP3, AUTS2, and RORA) associated with these SNPs were also highlighted in the UK Biobank database of 72 patients with primary aldosteronism (https://biobankengine.stanford.edu/coding/HC189). Of these, RORA has recently been found