Bisphenol A (BPA) and di(2-ethylhexyl) phthalate (DEHP), can induce long-lasting behavioral changes in rats. Additionally, changes in estrogen are correlated with the development of mood disorders in women; however, the underlying neurobiological mechanisms are unclear. This study was conducted to determine the cumulative effects of prenatal exposure to EDCs followed by chronic estradiol treatment in adult female rats on monoamine levels in the prefrontal cortex (PFC) and hippocampus (HC). Dams were orally administered saline (control; 10 μL/kg), BPA (B; 5 μg/kg), DEHP (D; 7.5 mg/kg) or a combination of BPA+DEHP (B+D) during days 6 through 21 of pregnancy. Adult female offspring were sham-implanted or implanted with pellets that release 17β-estradiol (E2) for 90 days (20 ng/day; Innovative Research America). The offspring then underwent a battery of behavioral tests at the end of treatment. Brains collected from the offspring were sectioned and the PFC and HC were microdissected and analyzed for levels of norepinephrine (NE), dopamine (DA) and serotonin (5-HT), using High-Performance Liquid Chromatography (HPLC). Significant reductions in monoamine levels were observed in the PFC while NE and 5-HT levels were markedly reduced in the HC after prenatal exposure to D or BD. BPA's effects on monoamines were comparatively modest. E2 exposure increased DA but decreased 5-HT levels in the PFC of control animals. Prenatal exposure to EDCs made the offspring non-responsive to E2. The marked reduction in monoamine levels could have implications for learning and memory.

Genetics and Development (including Gene Regulation)

ENDOCRINE DISRUPTING CHEMICALS

Prenatal Exposure to Bisphenol A, S and F Increases Blood Pressure in Female Rats

Maryam H. Al Mansi, BS1, YinJun Chuang, PhD1, Puliyur S. MohanKumar, BVSc, PhD2, Sheba M J MohanKumar, MS, BVSc, PhD2.
1UNIVERSITY OF GEORGIA, Athens, GA, USA, 2Univ of Georgia, Athens, GA, USA.

SAT-719

Cardiovascular diseases are the leading causes of mortality among men and women. With the new blood pressure guidelines from the American Heart Association, almost half of the United States population has hypertension (45.6%). The reasons for this high prevalence of hypertension in our population could be several, but the effect of emerging contaminants are overlooked and understudied. Bisphenol-A (BPA) is a widely used plasticizing agent that contaminates the environment. Most humans are exposed to BPA on a daily basis and urine levels of this endocrine disrupting chemical (EDC) are positively correlated with hypertension. The FDA banned the use of BPA in baby bottles in 2012, however, it is still being used in food containers and plastics. Currently, several BPA analogs such as bisphenol-S (BPS) and bisphenol-F (BPF) are used to replace BPA in the plastic industry. But their physiological effects are not clear. In order to study the effects of these EDCs on the development of hypertension, we exposed pregnant Sprague Dawley (SD) rats to saline, 5 μg/Kg BW of BPA, BPS or 1μg/kg BW of BPF. The offspring were allowed to reach adulthood before implantation with a radiotelemeter (Data Sciences International; HD-S10) in the femoral artery for undisturbed monitoring of systolic, diastolic and mean arterial blood pressure and heart rate. Recordings were measured once a week for 11 weeks over 24 hours to establish day and night readings. Night-time systolic BP was significantly elevated in BPA, BPF and BPS exposed rats compared to control. During the day, systolic BP was significantly higher in the BPA group compared to control. Diastolic BP was elevated in the BPS and BPF groups. Heart rate was elevated the most in the BPS group. These results indicate that prenatal exposure to low levels of BPA analogs has a profound effect on hypertension.

Tumor Biology

ENDOCRINE NEOPLASIA CASE REPORTS I

Familial Paraganglioma Syndrome: A Rare Case of Secondary Hypertension in Young People

Gonzalo Miranda, MD.
Dos de Mayo Hospital, Lima, Peru.

SUN-920

FAMILIAL PARAGANGLIOMA SYNDROME: A RARE CASE OF SECONDARY HYPERTENSION IN YOUNG PEOPLE

Paragangliomas are rare tumors originating in the autonomic nervous system, whose clinical manifestations are the result of excessive production of catecholamines.

We present a case of a 26-year-old female with 5 years of disease characterized by episodic profuse sweating, headaches and high blood pressure refractory to antihypertensive treatment. She also had intermittent palpitations which intensified 1 month before admission. Patient was cataloged with diagnosis of endocrine hypertension. She had elevated urinary fractionated metanephrines, elevated plasma normetanephrin and plasma chromогranin A (CgA).

Subsequently, an abdominal CT study was performed, finding a solid ovarian mass of defined edges located in retroperitoneal space, an intercave region immediately preceding the L2-L3 intervertebral disc that measured 26.2 x 23.9 x 28.8 mm. It was also found bilateral tumours at cervical level of 14 mm in right side and 10 mm in left side, suggestive of paranganglioma by magnetic resonance imaging (MRI).

With a suspected diagnosis of paranganglioma of Zuckerkandl’s organ, beta and alpha-adrenergic blockage were carried out and surgical intervention was done by a block resection of the tumour. Anatomopathological diagnosis confirmed the suspicion of well-delimited capsulated paranganglioma of 2.0 X 1.0 X 0.3 cm, with low mitotic index (<2) and a result of positive sinaptophisin by immunohistochemistry. She reached complete remission and normal determinations in urine of catecholamines and metanephrines. Currently the patient is in follow-up with favorable evolution and succinate dehydrogenase type B (SDHB) gene test is pending.

Despite infrequency of parangangliomas, it is important to take them into account in the differential diagnosis of
Adipose Tissue, Appetite, and Obesity
ADIPOSE TISSUE BIOLOGY AND OBESITY II
PAPP-A Inhibition - a Novel Anti-Obesity Therapeutic Approach
Akhila Ramakrishna, MD, Cheryl A. Conover, PhD.
Mayo Clinic, Rochester, MN, USA.

SUN-591
Background: Adipose tissue is a heterogeneous endocrine organ with tremendous capability for expansion. The antithetical pathogenicity of visceral adipose tissue (VAT), compared to subcutaneous adipose tissue (SAT), has been linked to the metabolic stress of enlarging mature adipocytes and a limited ability to recruit new adipocytes. One of the major distinguishing features of VAT preadipocytes is the high expression of Pregnancy Associated Plasma Protein–A (PAPP-A) when compared to SAT. PAPP-A is a zinc metalloprotease that is secreted, and can associate with the cell surface in an autocrine or paracrine fashion. It is the only known physiological IGFBP-4 (Insulin-like Growth Factor Binding Protein) protease. It cleaves the IGFI/IGFBP-4 complex, releasing IGF, making it more bio-available for receptor engagement and downstream signaling. The role of IGFs in adipogenic differentiation is well established. While there is quantitative depot-specific variability in PAPP-A expression among preadipocytes, mature adipocytes do not express any PAPP-A. These findings suggest that there may be a relationship between PAPP-A inhibition and adipogenic differentiation and maturation. Similar to human VAT, PAPP-A expression is highest in visceral fat in murine models. The PAPP-A KO mice, when fed a high fat diet, showed restrained visceral adiposity and decreased visceral adipocyte size, suggesting that PAPP-A could regulate adipogenesis locally in tissues that express high PAPP-A.

Hypothesis: PAPP-A inhibition is a novel anti-obesity treatment strategy. Methods/Results: We fed 20 male and 20 female wild type mice 42% high fat diet (HFD) starting at 10 weeks of age. Concomitantly, we treated 10 mice in each group with either mAb-PA1/41 (a PAPP-A neutralizing monoclonal antibody) or IgG2a (control isotope), intraperitoneally at a dose of 30 mg/kg weekly for the duration of the HFD. At the end of 15 weeks, the mice were sacrificed and the adipose tissue, serum and solid organs were harvested.

Compared to the control (IgG2a) mice, the mAb-PA1/41 treated male and female mice gained 40% less weight (P = 0.03) and had smaller visceral fat depots (mesenteric and pericardial). Also, when we looked at individual adipocyte size, the drug treated mice had 45% smaller mesenteric adipocytes (P = 0.002) and 44% smaller pericardial adipocytes (P= 0.003). Also, the visceral depots in the drug treated mice had 30% more cells (P = 0.006). In both groups, there was decreased liver lipid content (P=0.005). The mAb-PA1/41 treatment had no significant effect on subcutaneous fat depots.

Conclusion: Pharmacologic inhibition of PAPP-A decreased weight gain, visceral fat depot weight, visceral adipocyte size, hepatic lipid deposition and increased visceral adipocyte cell number in both male and female mice that were fed a high fat diet.

Thyroid
THYROID NEOPLASIA AND CANCER
In Silico Analysis of rs1042522 and rs1042522 Polymorphic Variants of TP53 Gene
Izabela Dal Bô, Bsc, Larissa Teodoro, Msc, Karina Colombera Peres, Msc, Elisangela Souza Teixeira, Bsc, Natassia Elena Bufalo, PhD, Laura Sterian Ward, MD, PhD.
Laboratory of Cancer Molecular Genetics, Faculty of Medical Sciences, University of Campinas (Unicamp), Campinas/SP, Brazil.

MON-519
The TP53 gene encodes the p53 protein which is a nuclear phosphoprotein that plays a key role in cell cycle regulation, especially in the transition from G0 to G1. It is located on chromosome 17 at position p13.1 and found at very low levels in normal cells, but it is expressed in large quantities in damaged cells. The most frequent alterations in the TP53 gene are point mutations that cause alteration in the base sequence, resulting in a defective protein. The most frequent alteration occurs in codon 72 (rs1042522). P72R shows an exon 4 polymorphism of the TP53 gene where it there is a substitution of an arginine (Arg) by a proline (Pro). This variant is associated with sporadic thyroid cancer. In addition, codon 72 variants decrease p53’s ability to activate apoptosis and are associated with some autoimmune diseases like Graves’ disease. The codon variant 47 (rs1800371) P47S has a rare polymorphism in the p53 N-terminal transactivation domain that replaces the serine-like wild-type proline (Ser). This variant is associated with sporadic thyroid cancer. In addition, codon 72 variants decrease p53’s ability to activate apoptosis and are associated with some autoimmune diseases like Graves’ disease. The codon variant 47 (rs1800371) P47S has a rare polymorphism in the p53 N-terminal transactivation domain that replaces the serine-like wild-type proline (Ser). This variant is associated with sporadic thyroid cancer.

In order to better understand the role of SNPs (rs1042522) and (rs1800371), based on data obtained from the NCBI dbSNP database and UniProt, we evaluated the effect of amino acid alteration on protein structure. We used bioinformatics tools such as SIFT (Sorting Intolerant from Tolerant), Align GVGD, PolyPhen-2, SNAP (Screening for nonacceptable polymorphisms), PANTHER (Protein Analysis Through Evolutionary Relationships), PredictSNP, nsSNPAnalyzer, PROVEAN, SNPs & GO, PMut and MuPRO. Rs1042522 and rs1800371 bioinformatic analysis suggested that the amino acid change alters protein structure (Align GVGD tool), decreases the stability (MuPro tool) and function (SNAP) of the protein. SNPs & GO confirmed an association of these polymorphisms with different diseases. We conclude that SNPs rs1042522 and rs1800371 are important in the process of tumorigenesis, corroborating findings from our group and others that suggest that they difficult the action of p53 protein.