of pro-inflammatory cytokine IL-8. Our research also showed that addition of IL-8 (1 ng/ml) to melanoma cells stimulated cell growth (117%) and suppression of IL-8 by curcumin (100 μM) pre-treatment suppressed human melanoma cell growth (26%) in-vitro. This observation prompted us to check the effect of male sex hormones androstenedione (AD) and testosterone (T) on melanoma cell growth. AD and T also suppressed cell growth and IL-8 secretion, but not as significantly as that of progesterone. However, addition of progesterone (10 μM) along with androgens showed an additive effect on the inhibition of melanoma cell growth and suppression of IL-8 secretion. As steroids (P, AD, T) targeted IL-8 for their action, it was decided to check whether vitamin-D3 also targeted IL-8 secretion and cell growth. Active form of vit-D3 (25 μM) also suppressed IL-8 secretion and cell growth. But, addition of progesterone (50 μM) along with D3 significantly suppressed cell growth and IL-8 secretion. This brought IL-8 into focus as a key molecule regulating melanoma cell growth. In order to check whether IL-8 was *the molecule* involved in regulating melanoma cell growth, IL-8 rescue experiment after curcumin (25 μM) pre-treatment was carried out. IL-8 (100 ng/ml) was able to rescue cell growth completely after pre-treatment with curcumin, suggesting IL-8 was the molecule involved in regulating melanoma cell growth. Literature also suggested important role for IL-8 in regulating melanoma cell growth. Conditional expression of IL-8 in nude mouse by Dr. Singh et al., indicated in-vivo role of IL-8 in melanoma growth and metastasis. **Conclusion:** Both, in-vitro and in-vivo studies suggested an important role for IL-8 in regulating melanoma growth and metastasis. So, IL-8 could be targeted to arrest melanoma growth and metastasis in-vivo. *Hence, IL-8 could be a potential target for melanoma treatment.*

Reproductive Endocrinology

FEMALE REPRODUCTION: BASIC MECHANISMS

Ovulation Induction Results in Altered Growth and Metabolic Dysfunction in Mice Offspring

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MON-LB001

Nearly 15% of couples are affected by infertility and a large proportion of individuals will need to use ovulation induction (OI) or assisted reproductive technologies (ARTs) to conceive. Previous studies have shown that offspring conceived by ARTs are predisposed towards increased insulin resistance and glucose intolerance. However, the long-term effects of OI alone on offspring health have not been studied. This rodent study was designed to elucidate the effects of maternal superovulation on offspring growth and development.

C57Bl/6 females were either naturally mated (control= C) or super-ovulated (5 IU PMSG; 5IU hCG, OI group) and mated to C57Bl/6 males with one Agouti viable yellow (Avy) allelic mutation. The Avy allele contains an intracisternal A particle whose methylation levels determine expression of the agouti protein which alters coat color and can be used as a phenotypic readout for global methylation. Offspring (n= 108 control and n = 69 OI) were followed through 13 weeks of age to measure birth parameters, growth rate, fasting glucose, GTT, and body composition (EchoMRI). Parametric and non-parametric tests were used as indicated. Only results with $p<0.05$ are reported.

Results: Surprisingly, while litter size was not different (C = 7, OI = 6), superovulated mothers had fewer surviving pups (C=6.5 pups, OI=5 pups). No major differences in coat color frequencies were observed between the two groups, suggesting no changes in DNA methylation. All OI pups had decreased anogenital distance (males C = 2.1mm, OI = 1.7mm; females C = 1.74mm, OI = 1.48mm), while OI female had lower birthweights (C = 1.38g and OI = 1.23g). Starting at four weeks of age, OI male had lower weight compared to control males. As early as 3 weeks, significant differences in fasting glucose levels were noted (C = 162 mg/dL, OI = 149.5mg/dL). Additionally, superovulated males had lower lean mass at 8 weeks of age (tested by EchoMRI: C = 23.6g, OI = 19.3g) and higher insulin levels at 13 weeks (120 min post injection, C = 339 mg/dL, OI = 213 mg/dL). In summary, we found that the process of OI alone has profound effects on offspring development in a sexual dimorphic fashion. Additional studies will be performed up to 30 weeks of age. Funding: R01 HD092267-01to P

Genetics and Development (including Gene Regulation)

ENDOCRINE DISRUPTING CHEMICALS

Examination of Hepatic Gene Expression Following Developmental Exposure to Dieldrin in Trachemys Scripta and Discovery of a Novel Hepacivirus

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SAT-LB131

The Massachusetts Military Reservation (MMR) is a Superfund site where ground water has been contaminated by a mixture of pollutants. Exposure to these chemicals is a public health concern and reproductive impairments have been observed in a population of turtles (*Chrysemys picta*) endemic to this site. We hypothesize that developmental exposure to endocrine disrupting compounds originating from the MMR might lead to abnormalities seen in adult animals. Upon examination of egg yolk from turtles at the impacted site, we found the presence of dieldrin and *p,p'*-DDE. Turtles from a reference site were also found to have *p,p'*-DDE present in the yolk. In order to investigate these chemicals in the laboratory we used a closely related turtle (*Trachemys scripta*) and applied vehicle, dieldrin, or *p,p'*-DDE to the eggshells. Absorption of *p,p'*-DDE through the eggshell was limited. Although there were variations in absorbance, we were able to achieve levels of dieldrin in the yolk similar to what was seen in animals from the impacted site. Following *in ovo* exposure to dieldrin, we used RNAseq to examine hepatic gene expression in neonates and found that several transcripts were repressed at least 1.5-fold in the dieldrin-treated animals. QPCR was carried out to

confirm differences in gene expression. We found that hepatic gene expression (fold ± SEM) of Gamma-Butyrobetaine Hydroxylase 1 (*Bbox1*) was higher in vehicle-treated animals (1 ± 0.60) compared to dieldrin-treated animals (0.29 ± 0.12). *Bbox1* catalyzes the last step in the L-carnitine biosynthetic pathway, which is necessary for mitochondrial beta-oxidation. Dieldrin-induced reduction in L-carnitine production may be a critical factor in adult reproductive function. Further, Protein-L-Isoaspartate (D-Aspartate) O-Methyltransferase Domain Containing Protein 1 (*Pcmtd1*) was higher (1± 0.76) in vehicle-treated animals compared to dieldrin-treated animals (0.13 ± 0.044), and DENN Domain Containing 5B (*Dennd5b*) was also found to be higher in vehicle-treated (1 ± 0.39) compared to dieldrin-treated (0.28 ± 0.10) turtles. We found that dieldrin exposure did not alter gene expression of Cytochrome p450 1a (*Cyp1a*) a marker of aryl hydrocarbon receptor signaling, or Vitellogenin 2 (*Vtg2*) a marker of estrogen signaling. In our RNAseq analysis we unexpectedly discovered a *hepacivirus* infecting *T. scripta*. In the dieldrin-treated group, we used QPCR to examine gene expression of potential markers of *hepacivirus* infection. Neither Interleukin 1 Beta (*Il-1*β), SMAD Family Member 6 (*Smad6*), C-C Motif Chemokine Ligand 5 (*Ccl5*), or TNF Receptor Superfamily Member 9 (*Tnfrsf9*) was found to differ in turtles carrying the virus, compared to non-infected animals. In conclusion, we found that developmental dieldrin exposure of *T. scripta* slightly reduces neonatal expression of several gene transcripts which may be correlated to adult reproductive fitness.

Adrenal

ADRENAL CASE REPORTS II

Using Chromogranin A to Unmask the Great Masquerader: A Case Reportof a Minimally Symptomatic Pheochromocytoma

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SUN-LB35

Introduction/Background: Pheochromocytomas are rare neoplasms, occurring in less than 0.2% of the population. The classic triad of symptoms includes hypertension, headaches and sweating. An increasing number of patients with pheochromocytomas that are diagnosed at a pre-symptomatic stage.***Clinical Case*** A 69 yo male being worked up for hematuria and possible bladder cancer was referred to endocrinology due to a 3 cm x 3 cm right adrenal "incidentaloma." The mass was noted to be heterogeneously enhancing on CT adrenal protocol, suggesting pheochromocytoma, adrenal carcinoma or metastasis. He endorsed no clinical symptoms of hormone excess and blood pressure was controlled HCTZ. He was found to have elevated serum metanephrines (184 pg/mL, nl <57) and noremetanephrine (608 pg/dL, nl <148) and total metanephrines (792 pg/dL, nl <205). Other hormonal determinations were normal including cortisol (9AM, 8.97 ug/dL, nl 3-22), DHEAS 66 mcg/dL (25-240), estradiol 23 pg/mL (<39), 17 OHD 60 ng/dL, ACTH 37 (6-50), free testosterone 43.6, total testosterone 396, androstenedione 63 (20-220). Further testing revealed 24 hour urine metanephrine and catecholeamines; urinary metanehrine 2025, noremetanephrine 1729, total 2442 and epinephrine 48, norepinephrine 336 and dopamine 112 which were 2-3 times the upper limit of normal. Because the patient consumed significant amount of caffeine (10 cups of coffee and cola daily), these studies were repeated after caffeine washout. Repeat serum testing revealed metanephrine at the upper limit of normal (metanephrine 47, noremetanphrine 146, respectively). Chromogranin A levels were elevated before (626 units) and after PPI discontinuation, (539 units, nl 25-140). Given the biochemical results and size of mass, he was referred him surgical resection. He was treated pre-operatively with doxazosin and underwent an uncomplicated right adrenalectomy via posterior right retroperitoneoscopic. Pathology was consistent with pheochromocytoma without capsular invasion. Immunohistochemical stains were characteristic of pheochromocytoma, positive for synaptophysin, chromogranin, and S100 but negative for Cytokeratin AE1/AE3 and calretinin. ***Conclusion:*** We present the case of a patient with a clinically asymptomatic pheochromocytoma. The diagnosis was supported by elevations in chromogranin and catecholamine metabolites, although the latter results were mixed and clouded by potential confounding factors such as heavy caffeine intake. The case demonstrates that with early detection, screening should include patients with no symptoms and otherwise low risk of disease. Decisions on surgical resection should be based on clinical suspicion, symptoms, imaging, tumor size and biochemical findings given the aggressive nature of these tumors and their malignant potential.

Steroid Hormones and Receptors

STEROID BIOLOGY AND ACTION

The LncRNA Growth Arrest Specific 5 Regulates Cell Survival via Distinct Structural Modules With Independent Functions

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SAT-LB138

The growth arrest-specific 5 (*gas5*) gene encodes a long non-coding RNA (lncRNA) that is required for normal growth arrest, slows down the cell cycle, controls apoptosis, and is required for the inhibition of cell growth by mTOR inhibitors such as rapamycin. In agreement with this role in regulating cell proliferation, Gas5 expression is reduced and acts as a tumor suppressor in numerous cancers, including B-cell lymphoma and leukemia. At its 3' terminal end (nucleotides 546-566) Gas5 contains a predicted stem-loop structure that specifically interacts with steroid receptors (SRs) and blocks DNA-dependent steroid signalling. In steroid-sensitive cancer cells such as prostate cancers this SR binding motif is responsible for Gas5 effects on cell growth. This is not true in other cell types, however, where proliferation is not strongly dependent on SR signaling (e.g. leukemic T cells). Therefore, other regions in