APNtg offspring from APNtg dams were protected against this effect. Visceral adipose tissue gene expression was unaltered in PNA wt offspring, regardless of the dam’s genotype, while APNtg offspring, regardless of PNA, had increased expression of adipogenic genes. Anogenital distance was increased in all PNA wt offspring independent of the dam’s genotype. There was, however, no difference between APNtg-vehicle and APNtg-PNA mice, suggesting that adiponectin overexpression protects against this effect. PNA leads to disrupted estrous cycle and fewer ovulations, but this effect was less pronounced in PNA wt mice from APNtg dams. Our data suggests that elevated maternal adiponectin protects the offspring against PNA induced metabolic dysfunction, and to a lesser extent reproductive dysfunction.

Genetics and Development (including Gene Regulation)

**GENETICS AND DEVELOPMENT AND NON-STEROID HORMONE SIGNALING I**

**Prevalence of Renal Cysts in Patients with Carney Complex**

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**SUN-713**

In the general population renal cysts appear most commonly in patients >50 y and in men. Among published studies, the prevalence of renal cysts detected by MRI was 27%, detected by CT was 20-41%, and detected by US was 4-17% (Mensel, et al., 2018; Choi, et al., 2016). In these studies, the male to female ratio in patients with renal cysts ranged from 1.4:1 to 2.9:3:1. Carney complex (CNC) is an autosomal dominant multiple endocrine neoplasia and lentigiosis syndrome predominantly caused by aberrant cAMP-protein kinase A (PKA) signaling mostly (but not always) due to germline inactivating defects in PRKARIA which encodes the regulatory subunit type 1α of PKA. In a small retrospective study, 5 of 9 subjects with CNC had renal cysts on MRI or CT (Ye, et al., 2017). This same study evaluated the development of renal cysts in kidney-specific Prkar1a knockout mice, where all mice developed a renal cystic phenotype. To determine the prevalence of renal cysts, we performed a retrospective cohort study of patients with CNC evaluated at our institution between 1984 and 2019 who underwent renal imaging with MRI, CT, and/or US. We hypothesized that CNC leads to renal formation of cysts in humans, with increased number of renal cysts and earlier age at detection. 117 patients with CNC (69 female [59%], 48 male [41%]) were evaluated with renal imaging (56% MRI, 41% CT, 3% US). Of these, 39 (33%) patients had renal cysts that were first detected on imaging between the ages of 13 and 58 y (mean age at diagnosis 37.1 ±12.7 y; 5 [13%] 12-19 y, 5 [13%] 20-29 y, 10 [26%] 30-39 y, 11 [28%] 40-49 y, and 8 [21%] 50-59 y). The mean number of cysts was 1.3 ±0.7, and mean dominant cyst size was 1.2 ±0.9 cm. Average creatinine at diagnosis was 0.8 ±0.2 mg/dL. Of the patients with renal cysts, 22 were...
female (56% of patients with renal cysts, 32% of females with CNC that underwent renal imaging) and 17 were male (44% of patients with renal cysts, 35% of males with CNC that underwent renal imaging). There was no difference in the prevalence of renal cysts between males and females (35% vs 32%, p=.70, for a 1:1 ratio). Age, number, and dominant cyst size were also not different between sexes (p=.51, p=.84, and p=.26, respectively). However, creatinine levels were higher in males (0.9 ±0.1 vs 0.7 ±0.1, p<.001). All 39 patients with renal cysts had defects in PRKARIA as compared to 73 of 78 (94%) patients with CNC that did not have renal cysts on imaging (p=.17). In conclusion, our data demonstrate that there is a high prevalence of renal cysts in patients with CNC with both males and females being affected equally, in contrast to the majority of previously reported population studies. They also suggest that renal cysts may develop in patients with CNC at a younger age. These results can be further validated by comparison to a cohort of healthy controls.

**Genetics and Development (including Gene Regulation)**

**GENETICS AND DEVELOPMENT AND NON-STEROID HORMONE SIGNALING II**

**Induction of Apolipoprotein A1 Gene Expression by the Rare Sugar Allulose**

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**MON-711**

Apolipoprotein A-I (apo A-I) is the primary protein component of high-density lipoprotein (HDL) and has many well-documented properties which promote cardiovascular health. However, clinical trials designed to increase HDL levels by preventing its catabolism have failed in their primary endpoints in decreasing the risk of cardiovascular disease. Alternative strategies to increase de-novo apo A-I production may be more attractive. We recently demonstrated that the rare sugar allulose decreases oxidative stress and endoplasmic reticulum stress in both endothelial cells and hepatocytes. During these studies we demonstrated that allulose also induces apo A-I secretion by HepG2 cells. Apo A-I, albumin, and SP1 levels were measured by Western blot. Apo A-I and glyceraldehyde-3-phosphate (GAPDH) mRNA levels were measured by quantitative real-time polymerase chain reaction. The effect of allulose on apo A-I promoter activity was measured using transient transfection assays with several plasmids containing various segments and mutations in the apo A-I gene promoter. Apo A-I protein and mRNA levels in cells treated with allulose increased more than two-fold in a dose-dependent manner. These changes were due to the ability of allulose to induce apo A-I gene promoter activity. Using a series of deletion constructs, an allulose-response element was identified in the apo A-I gene promoter which was previously shown to confer induction of apo A-I gene expression by insulin and epidermal growth factor (EGF), the insulin response core element (IRCE). Mutation of the IRCE decreased the ability of allulose and insulin to induce apo A-I promoter activity. Allulose treatment also increased expression of the transcription factor SP1, which had been shown previously to be essential for the effects of insulin and EGF on apo A-I promoter activity. In conclusion, allulose increased apo A-I gene expression in HepG2 hepatocytes. This effect was mediated by the IRCE in the apo A-I gene promoter and the transcription factor SP1. The rare sugar allulose may have novel anti-atherogenic properties, in part, by increasing HDL levels.

**Thyroid**

**THYROID DISORDERS CASE REPORTS II**

**Thyroid Dysfunction in a Patient with Malignant Melanoma Treated with Immune Checkpoint Blockade**

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**SAT-473**

Thyroid Dysfunction in a Patient with Malignant Melanoma Treated with Immune Checkpoint Blockade

**Background:** Thyroid dysfunction is a known immune-related adverse event associated with immune checkpoint inhibitor therapy.

**Clinical Case:** 48 year old female, newly diagnosed with metastatic melanoma started on combination immune checkpoint inhibitor therapy with Ipilimumab and Nivolumab. Her baseline thyroid function tests were normal. 6 weeks after the first cycle, she was found to have TSH of 0.010IU/ml with FT4 3.33IU/ml. Patient was started on Prednisone for 2 weeks and beta-blocker for symptom control by oncology team and referred to endocrine clinic for further evaluation. She was diagnosed with thyroiditis. TSI and thyroid uptake scan were not checked as there was no clinical suspicion for Graves disease in the absence of ophthalmopathy and thyroid enlargement. Serial TFTs were obtained which showed improvement. However, 4 weeks later, patient developed overt hypothyroidism (TSH 11.800IU/ml, FT4 0.68IU/ml) for which therapy with levothyroxine was started.

**Conclusion:** Our case emphasizes the importance of close monitoring of patients receiving Immune Checkpoint Inhibitor Therapy for prompt diagnosis and management of the thyroid disorders to prevent complications such as thyroid storm or myxedema coma. Per the ASCO guidelines, Brahmer et al recommends monitoring TFTs every 4 to 6 weeks from the start of the therapy and every 2-3 weeks after the diagnosis to detect conversion of thyroiditis to hyperthyroidism. In the combination therapy, the median time to onset of hyperthyroidism and hypothyroidism after first treatment was 21 and 63 days and transition time from hyperthyroidism to hypothyroidism was 42 days.

**Reference:** (1) Characterization of Thyroid Disorders in Patients Receiving Immune Checkpoint Inhibition Therapy Lee et al

(2) Management of Immune-Related Adverse Events in Patients Treated With Immune Checkpoint Inhibitor Therapy: American Society of Clinical Oncology Clinical Practice Guideline

Julie R. Brahmer et al