Neuroendocrinology and Pituitary
ADVANCES IN NEUROENDOCRINOLOGY
Deletion of Hepatic Kisspeptin Results in Abnormal Glucose Metabolism in Female Mice
Bahaa Aloqaily, Ph.D., Hyokjoon Kwon, Ph.D., Ariel L. Negron, PhD, Fredric E. Wondisford, MD, Sally Radovick, MD.
Robert Wood Johnson Medical School/ Rutgers University, New Brunswick, NJ, USA.

SUN-261
Kisspeptin is a hypothalamic protein critical for neuroendocrine control of pubertal development and fertility and is modulated by nutritional signals. Kisspeptin has been localized to specific neurons located in the arcuate and anteroventral periventricular (AVPV) nuclei of the hypothalamus and is secreted to control GnRH mediated pubertal maturation and reproduction. Kisspeptin has also been localized to peripheral tissues including the liver, fat, gonads, intestine and placenta, although its role in these tissues is unclear. The objective of current study is to define the role of hepatic kisspeptin as a metabolic sensor. A floxed Kiss1 mouse has been developed, and ablation of liver-specific Kiss1 was achieved in two to three month old Kiss1f/f male and female mice given a single tail vein injection of thyroid hormone-binding globulin (TBG) promoter-driven Cre recombinase adenovirus-associated virus (AAV-CRE). A control group of Kiss1f/f male and female mice received an injection of AAV-GFP, expressing green fluorescent protein. Two weeks after injection, a glucose tolerance test (GTT) was performed followed by an insulin tolerance test. To determine whether changes had occurred in the reproductive axis, estrous cyclicity was assessed by daily vaginal smears and estrous cycle phases determined by vaginal cytology. Mice were euthanized four weeks post-injection and tissues were collected for RNA extraction and gene expression analysis via qRT-PCR. As expected, qRT-PCR data showed absence of Kiss1 expression in the liver of AAV-CRE mice compared to AAV-GFP mice with no changes in kisspeptin gene expression were noted in the ovary, testes, spleen, pancreas, arcuate or AVPV. Estrous cyclicity was also not affected by viral ablation of hepatic Kiss1. Elevated fasting glucose and glucose intolerance in the GTT were found in AAV-CRE compared to AAV-GFP females (P < 0.05). No differences in AAV-CRE and AAV-GFP male mice were found, indicating the importance of Kiss1 in glucose homeostasis in females. The insulin tolerance test was not statistically different between groups or treatments. Further research is required to elucidate the mechanism by which hepatic kisspeptin alters glucose metabolism in mice in a sexually-dimorphic fashion.

Diabetes Mellitus and Glucose Metabolism
GESTATIONAL DIABETES, DIABETES IN PREGNANCY, AND IN UTERO EXPOSURES
Sex-Specific Difference in REG3G Expression Directs the Maintenance of Islet Function in Offspring of Obese Mice
Jose Casasnovas, PhD, James C. Jarrell, BSc, Kok Lim Kua, MD.
1Indiana University School of Medicine, Indianapolis, IN,
SUN-640
Offspring exposed to maternal obesity are more likely to develop pancreatic islet dysfunction, but the underlying mechanistic pathway is unclear. We previously reported that fetal rats exposed to in-utero hyperglycemia had decreased fetal β-cell REG3G, and then developed lower β-cell mass and insulin secretion at adulthood. REG3G is reported to bind EXTL3 which initiates heparan sulfate (HS) synthesis size important for pancreatic islet integrity. In this study, we sought the delineate the impact of maternal obesity exposure in altering offspring islet Reg3g and HS, and determine how changes in Reg3g and HS alters offspring islet insulin secretion. We hypothesize that exposure to maternal obesity (MatOb) suppresses offspring β-cell REG3G leading to decreased HS affecting β-cell health/function. We induced maternal obesity by feeding female mice western style diet for 4 weeks, while control mice were fed with regular chow. Offspring were evaluated for fat body mass, glucose intolerance, insulin secretion at postnatal day 21 and at 2-month-old. MatOb mouse offspring had increased fat-to-lean ratio and glucose intolerance but no insulin resistance at postnatal day 21, indicating decreased islet function. We performed islet perfusion to measure insulin induced secretion in postnatal day 21 offsprings. We found that male offspring but not female had impaired insulin secretion. In 2-month old offspring fat-to-lean ratio persisted but only males presented glucose intolerance. We found that pancreatic islet Reg3g expression was higher in MatOb females than males. This was accompanied increased HS in pancreatic islets of MatOb females compared to males. All together our data indicates a sex-specific protective role of Reg3g/HS in pancreatic islet function.

Neuroendocrinology and Pituitary
NEUROENDOCRINOLOGY AND PITUITARY
Identification of IGF-1 Variants in a Clinical Study of 307,000 Specimens: Discrepancies with General Population and Novel Discoveries
Ievgen Motorykin, PhD, Michael John McPhaul, MD, Nigel J. Clarke, PhD, Zengru Wu, PhD
1Quest Diagnostics, San Juan Capistrano, CA, USA, 2Medical Director, Endocrinology, San Juan Capistrano, CA, USA, 3QUEST DIAGNOSTICS NICHOLS INST, San Juan Capistrano, CA, USA.

SUN-271
High resolution accurate mass (HRAM) mass spectrometry (MS) is a highly specific and robust method for identifying and quantifying intact IGF-1. However, protein variants with mass-to-charge ratios differing from wild type (WT) are not included in quantification. Previously, we developed a naming convention for isotopic peaks, called the Isotopic Peak Index (IP) that helps identify variants by comparing their IP's. This method cannot differentiate some variants; however, the relative retention time (rRT), which is defined as the difference between the chromatographic RT of a variant and that of the WT, may help in some cases. We report IGF-1 variants detected using rRT and IP; we also compare expected and observed frequency of common variants A67T and A70T. For IPi, 4 variant groups (VGs), each monitored at a single m/z ratio, were identified to make detection of 15 variants more efficient. Variants within each VG could be distinguished if they had different IP's. To distinguish some variants in the same VG with the same IPi, we used rRT. We also developed a tandem mass-spectrometry (MS/MS) method that uses specific fragment ions generated during fragmentation to distinguish between the most abundant variants, A67T and A70T. Of the 307,269 samples we analyzed, 1,266 (0.4%) variants were identified. IPi, identified variants with different indices and the rRT approach distinguished between pairs of variants that IPi could not. A38V vs A67V, R55K vs R36Q. The following variants (and their count) were identified: R50W/T4M/A67T/A70T (1,210), A67V (23, A38V (9), P66A (6), R36Q/R50Q (5), V17M/V44M (5), A67S (4), P55K/R56K (3), T29I/T41I (1), S34N (1), S33P (1), Y31H (1). We observed a different relative frequency of A67T and A70T variants than expected based on a general population ExAC DNA database. We expected to detect 2.1-fold more A67T than A70T counts. However, DNA sequencing of 74 samples in this study identified 1.6-fold more A70T occurrences (46) than A67T (28). Overrepresentation of A70T may suggest its clinical significance. The A38V variant was predicted to occur 5.1-times in the population studied, but it was detected 9 times. The A67V variant was not present in the ExAC database, but it was detected in 23 patients. We detected 2 variants that did not match WT or expected variants; DNA sequencing identified them as new variants (S33P, Y31H). DNA sequencing also identified new variants (R50Q, R56K, T41I) at different positions than expected. Using a few test samples, the tandem MS technique has shown its ability to distinguish between A67T and A70T. It will be applied to this patient set. IPi and rRT can be used together to identify and differentiate IGF-1 variants. Such an approach may provide improved estimates of variant frequencies and identify new variants.

Tumor Biology
ENDOCRINE NEOPLASIA CASE REPORTS I
The Rare Men of Mississippi Complications in the Diagnosis of Multiple Endocrine Neoplasia Type 1
Hytham Rashid, DO, MPH, Tiarra Clayton, DO, Kurt Bruckmeier, MD, Ben Drake, DO
Merit Health Wesley, Hattiesburg, MS, USA.

SUN-912
Background: Multiple endocrine neoplasia type 1 (MEN1) is a rare, autosomal dominant disorder associated with tumors of the parathyroid glands, pituitary gland, and gastroenteropancreatic cells caused by mutations of the MEN1 tumor-suppressor gene. Thescarcity with which this syndrome is encountered makes diagnosis challenging in rural settings.
Clinical Case: A 34-year-old male presented to the Emergency Department complaining of intermittent abdominal pain for the past year, that was associated with nausea, vomiting, and diarrhea. Past medical history was significant for hyperparathyroidism treated with