insulin is the only effective treatment, but there is still no cure or interventional therapy available to inhibit progression of T1D. Successful T1D interventional therapy must protect pancreatic beta cells from autoimmunity while enhancing beta cell survival and function. Our data suggest Cornus officinalis (CO) may be a candidate for interventional therapy to protect pancreatic beta cells from autoimmune attack and increase their function. CO has been used in traditional Chinese medicine (TCM) for over 2,000 years and has shown characteristics of anti-diabetic effects in vitro and in vivo but never examined in the application of T1D. Our prior publication (Mol. and Cell. Endo. 2019;494:110491), has shown increased proliferation and protection against Th1 cytokine attack upon CO treatment using a human pancreatic beta cell line, 1.1B4. From this, we sought to define precise molecular mechanism by employing a global and phosphorylation mass spectrometry (MS) approach. We applied CO to 1.1B4 cells for 2, 6, 12, and 24h then collected the cell lysates for MS analysis. Our global MS analysis revealed a 12-fold increase in beta cell functional regulator, IGFBP2, at multiple time points. IGFBP2 has been shown to display a T2D protective effect and regulate glucose metabolism. The ingenuity pathway analysis program (IPA) predicted an increase in insulin starting at 2h and the NRF2-mediated oxidative stress pathway at 12h and 24h. Furthermore, NRF2 is an upstream regulator of P62 which was significantly hyperphosphorylated at multiple timepoints from our MS analysis. Nrf2 is responsible for activating antioxidant enzymes upon oxidative stress, which is caused by proinflammatory cytokines in T1D. P62 aids in this pathway by targeting proteins for autophagy upon oxidative stress in order to keep cellular homeostasis within beta cells rather than cells progressing through apoptosis. Autophagy is critical for beta cell function and survival as it promotes survival under beta cell stress which would otherwise lead to cell death. The recovery and protection of autophagy in beta cells of patients in the pre-diagnosed stages of T1D could provide a beneficial interventional therapy in order to delay or inhibit the onset of T1D. Altogether, our proteomic analysis revealed an increase in IGFBP2 and predicted an increase in the NNR2-mediated oxidative stress pathway upon CO induction. Further analysis will examine the IGFBP2 and Nrf2-mediated oxidative pathway as a mechanism of CO induced protective and proliferative effects in pancreatic beta cells.

Reproductive Endocrinology

HYPERANDROGENISM

Metformin-Fish Oil Adjunct Therapy Improves apoB-Remnant Lipoprotein and Triglyceride Levels in Women with Polycystic Ovary Syndrome

Ethan Proctor, BSc1, Olivia Weaver, BSc1, Mahua Ghosh, Dr, PhD, FRCPC1, Katerina Maximova, Dr, PhD1, Spencer Proctor, Dr, PhD1, Donna Vine, Dr, PhD1.

1Univ of Alberta, Edmonton, AB, Canada, 2University of Alberta, Edmonton, AB, Canada.

SUN-022

Background: Polycystic ovary syndrome (PCOS) is highly associated with the metabolic syndrome (MetS): obesity, insulin resistance and atherogenic dyslipidemia. Women with PCOS-MetS are at higher risk of developing ischemic cardiovascular disease (CVD) and Type-2 Diabetes. First-line intervention in PCOS-MetS includes targeting diet and lifestyle, and metformin is commonly prescribed to treat insulin resistance, however these interventions have shown limited effectiveness to improve dyslipidemia. At present there are limited safe and efficacious options to target atherogenic dyslipidemia in young women with PCOS. Fish oil (FO) and Icosapentyl ethyl supplementation have been shown to reduce fasting TG, apoB and to improve ischemic CVD outcomes. The efficacy of FO or as an adjunct therapy to metformin to improve ApoB-remnant lipemia in PCOS-MetS is unknown. The aim of this pilot study was to determine the effect of metformin, FO and FO-metformin combination treatment on fasting and non-fasting plasma TG and apoB-remnant lipoprotein metabolism in patients with PCOS-MetS.

Methods: Participants diagnosed with PCOS aged 18-30yrs received dietary counselling and were randomly assigned to receive FO (n=8), metformin (n=7) or FO-metformin (n=12) treatment for 12 wks. Plasma lipids (TG and cholesterol), ApoB48 and ApoB100 lipoprotein metabolism were assessed in the fasting and non-fasting state using a standardized high-fat meal test.

Results: At baseline, the fasting plasma TG, ApoB48 and ApoB100 was 238.0 ± 21.0 mg/dL, 9.00 ± 1.12 ug/ml and 290 ± 18.00 mg/dL. FO and FO-metformin decreased fasting plasma TG by 10% and 30% compared to the metformin treatment group (7%). Fasting ApoB48 was reduced 45%, 16% and 19% in FO-metformin, FO and metformin treatment groups, respectively. Non-fasting plasma TG and apoB48 lipoprotein area under the curve were reduced by 30% in the FO-metformin treatment group.

Conclusion: These pilot findings demonstrate FO-metformin adjunct therapy may have greater efficacy to improve atherogenic apoB-dyslipidemia compared to metformin or FO alone in high-risk patients with PCOS-MetS. A larger clinical trial is warranted to determine the long term effects of FO-metformin intervention on apoB-dyslipidemia and atherosclerotic cardiovascular disease indices.

Reproductive Endocrinology

MALE REPRODUCTIVE health - FROM HORMONES TO GAMETES

Changes in Metabolic Parameters After Administration of Novel Oral Androgens with Progestational Activity for 28 Days

Fiona Yuen, MD1, Arthi Thirumalai, MBBS2, Ronald S. Suerdloff, MD1, Peter Y. Liu, PHD,MBBS1, Youngju Pak, PhD1, Laura Hull, BS1, Stephanie T. Page, MD, PhD1, Christina Wang, MD1.

1The Lundquist Institute, Torrance, CA, USA, 2University of Washington, Seattle, WA, USA.

SAT-040

Background: While the metabolic effects of testosterone have been well studied, the effects of co-administration of an androgen and progesterin are less established. Two novel compounds being investigated for male hormonal contraception, dimethandrolone undecanoate (DMAU)
and 11β-methyl-19-nortestosterone dodecylcarbonate (11β-MNTDC), have both androgenic and progestational activity.

Aim: Characterize the effects of DMAU and 11β-MNTDC on metabolic parameters including weight, lipid parameters, insulin resistance, and adiponectin.

Methods: Two randomized, double-blind, placebo-controlled studies in healthy men were performed to assess the safety and tolerability of DMAU and 11β-MNTDC taken orally for 28 days. Insulin and adiponectin assays were performed on a subset of banked samples. Changes in weight, LDL-C, HDL-C, fasting glucose, HOMA-IR, and adiponectin were assessed. Two way ANOVA with post hoc Tukey HSD was performed to assess for dosage (0, 200, or 400mg) and drug (DMAU or 11β-MNTDC) effects.

Results: A total of 85 subjects were included in this secondary analysis. There was a statistically significant decrease in HDL-C (mean change -1.1 and -1.5 mg/dL) and increase in weight (3 and 2 kg) and LDL-C (18 and 23 mg/dL) in the DMAU and 11β-MNTDC 400mg groups respectively. There was no significant difference between the 200 and 400 mg groups nor differences between the two androgens. There were no statistically significant changes in fasting glucose, adiponectin or HOMA-IR.

Conclusion: There were mild changes in weight, HDL-C, and LDL-C after 28 days of DMAU and 11β-MNTDC without significant changes in markers of insulin resistance or differences between the two compounds. Changes in metabolic parameters should be monitored and considered during further development of compounds for male hormonal contraception.

Neuroendocrinology and Pituitary

CASE REPORTS IN SECRETORY PITUITARY PATHOLOGIES, THEIR TREATMENTS AND OUTCOMES

Pituitary Macroadenoma Co-Secreting TSH and PRL Responsive to Cabergoline

Sarita Tirumalasetty, MD, Robert Galagan, Louisiana1, Dragana Lovre, MD, Julia David, MD

1Tulane University School of Medicine, New Orleans, LA, USA, 2Tulane University, Metairie, LA, USA.

SAT-272

Background: Thyroid-stimulating hormone (TSH) secreting tumors (TSHoma) account for 0.5-2% of all pituitary adenomas with a prevalence of 1-2 cases per million, indicating that TSHomas are very rare. The majority of TSHomas solely secrete TSH however 9.7% co-secrete Prolactin (PRL). We are reporting a case of co-secreting TSH and PRL pituitary macroadenoma responsive to Cabergoline (CAB) Case: A 52 year old multiparous female presented with symptoms of galactorrhea and amenorrhea. Lab investigation revealed elevated PRL 73 ng/mL (n [normal] = 1-24), Total T3 305 ng/dL (n = 71-180), Free T4 (FT4) 2.37 ng/dL (n = 0.6-1.15), TSH 6.09 UIU/mL (n = 0.5-5.0), and α subunit 7.7 ng/mL. Estradiol was low at 16.9 pg/mL and FSH 6.3 MIU/mL LH 1.7 MIU/mL. Visual field testing showed a right nasal step. MRI imaging demonstrated a 21x24x32mm pituitary macroadenoma with optic chiasm distortion. Partial Transsphenoidal surgery (TSS) was performed and immunostaining of tumor tissue was positive for PRL and negative for other pituitary hormones. One month post-surgical MRI revealed 14x17x15mm residual tumor. One month post-op TFTs were normal: TSH 0.99 ng/dL, FT4 0.61 ng/dL; PRL decreased to 34.8 ng/mL. Six month post-op TSH increased to 5.86 UIU/mL, FT4 1.43 ng/dL, and PRL 44.7 ng/mL. Two years post-op TSH 8.06 ng/dL with elevated α subunit 3.4 ng/mL and PRL 56.8 ng/mL. Octreotide was then initiated for TSHoma treatment however she was unable to tolerate the medication due to diarrhea so was switched to CAB. After starting CAB at 0.5mg twice a week, residual sellar mass increased in size to 19.5x16x23mm with TFTs: TSH 5.66 UIU/mL, FT4 2.48 ng/dL. CAB dose was eventually uptitrated to 1mg twice a week. Repeat MRI showed slight decrease in pituitary lesion to 19x21x18mm and downtrending TFTs: TSH 2.28 UIU/mL, FT4 1.17 ng/dL.

Discussion: In patients with pituitary tumors associated with elevated PRL and TSH, TSHoma should be part of the differential diagnosis. This patient’s initial lab evaluation with elevated PRL, TSH, FT4, Total T3, and α subunit confirm the diagnosis of a pituitary macroadenoma with co-secretion of PRL and TSH. Elevated PRL, TSH, FT4 and α subunit levels occurred 6 months after partial TSS resection with growing tumor size eventually requiring medical therapy. On CAB therapy, there were reductions in PRL, TSH, and FT4 levels as well as a decrease tumor size. This is the first reported case of a TSHoma responsive to CAB.

Neuroendocrinology and Pituitary

HYPOTHALAMIC-PITUITARY DEVELOPMENT AND FUNCTION

Mild Perinatal Undernutrition Results in Underweight Pups and a Premature Neonatal Leptin Surge

Tiffany K. Miles, B.S.1, Melody Lyn Allensworth, Ph.D2, Ana Rita Silva Moreira, MSc3, Angela Katherine Odle, Ph.D4, Anessa Haney, B.S.1, Alexandra Lagasse, B.S.1, Angus M. MacNicol, Ph.D5, Gwen V. Childa, PHD4

1University of Arkansas, Little Rock, AR, USA, 2Univ of Arkansas for Medical Sciences, Little Rock, AR, USA, 3University of Arkansas for Medical Sciences, Little Rock, AR, USA, 4Univ of AR Med Sci/Coll of Med, Little Rock, AR, USA.

SAT-287

Malnutrition causes dysregulated pituitary function, which may in part be due to lowered leptin signals. We showed that loss of somatotrope leptin receptors in mice reduces growth hormone (GH) secretion and promotes metabolic dysfunction in adults. More recently, we showed that adult male mice fasted for 12 or 24 hours also had significantly lowered GH secretion, which correlated with a 94% reduction in serum leptin. Malnutrition may result in changes in the leptin surge during neonatal development in rodents or the third trimester in humans. Severe (50% reduction) maternal undernutrition (1) blunted the surge in rodents, however less severe undernutrition (30% reduction) caused a premature leptin surge (2). Both studies reported that pups showed metabolic dysfunction as adults. In our studies of leptin regulation of somatotropes, we tested the more severe calorie restriction model and discovered significant