large volumes using thin section histology, there is a need for high resolution imaging and rendering of intact pancreatic tissue in 3D. **Aim:** To use optical clearing, whole organ imaging, and 3D rendering to quantify islets and innervation across the whole pancreas in healthy mice, in two mouse models of diabetes, and in pancreatic samples from nondiabetic and diabetic human donors. **Methods:** Whole-mount staining and clearing was performed using iDISCO+ to quantify innervation, defined by the neuronal marker NF200, and beta cells in pancreata from C57Bl/6 mice, non-obese diabetic (NOD) mice, streptozotocin (STZ)-treated mice, and in pancreatic samples from nondiabetic and diabetic human donors. Z-stacked optical sections were acquired with an Ultramicroscope II at 4x or 12x magnification. Imaris was used to create digital surfaces covering the NF200+ innervation and islets to automatically determine innervation density and islet/nerve interactions. **Results:** Beta cell volumes were 1-4% in the human pancreas, and 1-2% in the healthy mouse pancreas, with regional variations in islet volume and insulin intensity. There were also significant differences in islet biology between the diabetes models. Innervation of the endocrine pancreas was significantly enriched compared to the surrounding exocrine pancreas, with regional variation. Islets were closely associated with pancreatic innervation and decreased in size with increasing distance from nerves in both mouse and human pancreatic tissue. Innervated islets were relatively preserved in models of diabetes. Finally, islet innervation and expression of neural markers were higher in human samples from diabetic patients and in mouse models of diabetes, with temporal and regional differences. **Conclusions:** 3D imaging and unbiased analysis across the whole pancreas provides comprehensive measurement of pancreatic nerve volumes and distribution. It allows detailed analysis of the anatomical relationship between nerves and islets, and reveals a close association that is maintained across species. The relative enrichment of innervated islets in diabetes and dynamic changes in islet innervation during the development of diabetes suggest further work is needed to examine the role of pancreatic nerves in preserving and protecting beta cells.

Diabetes Mellitus and Glucose Metabolism

CLINICAL AND TRANSLATIONAL GLUCOSE METABOLISM AND DIABETES

The Effects of a High Intensity Glycemic Program on Weight and BMI

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MON-632

Background:
Multiple studies have shown that intensive glycemic control leads to improved HbA1c and delays the onset of complications in diabetes.[1] However, improvement in glycemic control has also been associated with weight gain.[1] The High A1C (HAC) program uses a multidisciplinary team to provide intensive therapy to patients with HbA1C ≥ 10% over 3 months to improve glycemic control. The aim of this retrospective study is to examine if the HAC program is associated with a significant change in weight and BMI.
Methods:
Patients enrolled in the HAC program were scheduled for frequent visits over the course of 3 months with an Endocrinologist, nurse practitioner, or diabetes educator. Data from patients with type 2 diabetes enrolled from March 2018 to June 2019 who attended at least 2 appointments was collected. Pre-enrollment HbA1c, weight, BMI, and total daily dose (TDD) of insulin (units/kg/day) were compared to post-enrollment using t-test analysis. Use of weight-lowering anti-hyperglycemic agents such as Metformin, GLP-1 agonists (GLP1A) and SGLT-2 inhibitors (SGLT2i) was collected.
Results:
44 patients were enrolled with 39/44 (88.6%) attending at least 2 visits and 5/44 (11.3%) who were lost to follow-up. The median HbA1c improved from 11.5% (9.7-14%) to 8.4% (5.9-14%), $p<0.001$.There was no significant change in mean weight (195lbs (110-360) vs 192lbs (114-358), $p=0.14$) or BMI (31 (20-49) vs 31 (21-49) kg/m^2, $p=0.86$). Pre-enrollment, 33/39 (84.6%) patients were on Metformin, 10/39 (25.6%) were on a GLP1A, and 3/39 (7.7%) were on a SGLT2i. At the end of the program, there were 34/39 (87%) patients on Metformin, 26/39 (66.6%) on a GLP1A, and 17/39 (43.5%) on a SGLT2i. There was no difference in the mean TDD of insulin at the start of the program of 0.63 units/kg/day (0-3.52 units/kg/day) compared to 0.60 units/kg/day (0-4.07 units/kg/day) at the end of the program ($p=0.97$).
Conclusions:
Patients enrolled in a high intensity glycemic control program had significant improvements in HbA1c without change in weight or BMI. Additional adjunctive non-insulin therapies and lifestyle management may be contributing factors for weight neutrality in our population. The significant improvement in HbA1c was not linked with increases in TDD of insulin.
Citation:
1."U.K. Prospective Diabetes Study Group: Intensive blood glucose control with sulfonylureas or insulin compared with convention treatment and risk of complications in patients with Type 2 Diabetes." *Lancet*, vol.353, 1998, pp.837-53.

Reproductive Endocrinology

MALE REPRODUCTIVE HEALTH - FROM HORMONES TO GAMETES

Linking Gonadotropin-Regulated Testicular RNA Helicase (GRTH/DDX25) to Histone Ubiquitination Network and Acetylation During Spermiogenesis

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SAT-031

Gonadotropin Regulated Testicular Helicase (GRTH/DDX25), a testis specific RNA helicase essential for the completion of spermatogenesis. Our early studies

discovered a missense mutation ($R^{242}H$) of GRTH gene in 5.8 % of a Japanese population with azoospermia. This mutation in COS-1 cells showed loss of the 61 kDa cytoplasmic phospho-species with preservation of the 56Kda nuclear non-phospho form of GRTH. Mice with knock-in (KI) of the human GRTH mutation, lack the phospho-form of GRTH, are sterile and lack sperm, with spermatogenic arrest at stage 8 of round spermatids. To determine the impact of phospho-GRTH on gene expression comparative studies of germ cells transcriptome profiles from WT and KI mice were conducted using Illumina RNA sequencing. RNA-Seq analysis revealed 1614 differentially expressed genes of which 886 down-regulated and 728 genes up-regulated genes. Gene Ontology analysis revealed several genes relevant to spermatogenesis, spermatid development and differentiation significantly downregulated. KEGG analysis showed genes related to Ubiquitin mediated proteolysis, protein processing in ER, RNA transport, Glycolysis pathways are down-regulated, and genes related to Focal adhesion and ECM interaction are up-regulated. RealTime-PCR analysis confirmed dramatic reduction in mRNA expression of ubiquitination related genes *Ube2j1*, *Ube2k*, *Ube2w*, *Rnf8*, *Rnf133*, *Rnf138* and increased expression of *Ccnd2*, *Col1a*, *Lamb1*, Cav1, *Igf1*, *Itga9* mRNA's in KI mice compared to WT. Western blot analysis revealed marked reduction in protein expression of UBE2J1, RNF8, RNF138 (ubiquitination network), MOF (histone acetyltransferase) and their modified Histone substrates (H2AUb, H2BUb), as well as H4Ac, H4K16Ac in KI mice. Immunohistochemistry analysis showed significantly reduced expression of RNF8, MOF, H4Ac and H4K16Ac in round spermatids of KI mice compared to WT. In KI mice absence of phospho-GRTH impairs RNF8 and MOF dependent ubiquitination and acetylation of histones required for histone replacement, chromatin condensation and spermatid elongation during spermiogenesis which finally results in germ cell arrest in step 8 of round spermatids. Thus, we conclude that phospho-GRTH affects the network which is critical for the replacement of histones during spermiogenesis.

Pediatric Endocrinology

PEDIATRIC GROWTH AND ADRENAL DISORDERS

Growth Hormone Deficiency in a Patient with Ectodermal Dysplasia

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SAT-108

Background information:
Ectodermal dysplasia (ED) is a rare heterogeneous group of genetic disorders of ectodermal derived tissues, characterized by abnormalities in skin, teeth, hair and eccrine glands. Growth failure in these children varies depending on the genetic mutation and has not been well characterized. This clinical case report presents a 11-year-old male with a heterozygous mutation in WNT 10 A, a variant of the hypohydrotic ED gene, who was found to have growth hormone (GH) deficiency and treated with GH.
Case report:
He was born at 35 weeks gestation by C-section with a birth weight of 5 lbs. 12 oz. to a mother who had invitro fertilization with donor eggs from the maternal aunt with ocular myasthenia gravis and sperm from the father. Pregnancy was complicated by twin gestation and polyhydraminos. He had transient myasthenia gravis and treated with pyridostigmine for 3 months for feeding problems and swallowing difficulty. He also had arthrogryposis of the distal upper extremities attributed to placental transfer of the maternal aunt's myasthenia gravis antibodies.
He was referred to the endocrine clinic for evaluation of his growth failure around the age of 8 years. His growth chart indicated that he grew along the 5thpercentile until age 5 year with a gradual decline to the 3rd percentile by age 7 year and close to 2nd percentile by age 8 year. His BMI was at 7th percentile. Mid parental height was 5'9". There was no history of delayed adolescence in the family. His twin sister had very mild form of arthrogryposis with dental delay but steady linear growth. He also had decreased exercise tolerance. His body tended to become hot during sports activities and had to wrap his face and neck with cold soaked towels. His other problems included delayed dental development with conical incisor, thin nail, missing teeth and hearing defects that raised suspicion for ectodermal dysplasia. Genetic testing at the age of 4 years had demonstrated a heterozygous mutation in the WNT 10A gene, an important gene for tooth development. Physical examination revealed a mild facial dysmorphism with conical incisor, missing teeth and high arched palate. He had contracture of the proximal inter phalangeal joints of the hands. Investigations revealed a normal thyroid function test, IGF-1 and IGFBP-3 level, CBC, sedimentation rate, chemistry panel and celiac titer. The bone age was concordant with his chronological age of 8 years. A GH stimulation study demonstrated a peak GH level of 4.94 ng/ml. An MRI of the brain revealed a normal pituitary gland. He was started on GH therapy with 0.3 mg/kg/week at age 9 year. His height improved from 2nd percentile at age 9 year to 20th percentile by age 11 year on growth hormone therapy. His exercise capacity and stamina also improved.
Conclusion:
Growth failure and GH axis should be evaluated in children with ED. GH therapy improves growth velocity and exercise capacity in patients with ED.

Cardiovascular Endocrinology

HYPERTRIGLYCERIDEMIA; INFLAMMATION AND MUSCLE METABOLISM IN OBESITY AND WEIGHT LOSS II

High Prevalence of Cardiometabolic Diseases and Abdominal Aortic Calcification in Psoriasis

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SUN-545

Psoriasis has been shown to increase the risk of cardiovascular disease. Studies indicate that the presence of