and the BioBreeding (BB) rat have identified a peripheral inflammatory state associated with diabetes susceptibility that is consistent with microbial antigen exposure and pattern recognition receptor ligation. *Lactobacillus plantarum* 299v (Lp299v), a probiotic strain, is reported to increase plasma and stool levels of anti-inflammatory short chain fatty acids (SCFA) and promote IL-10 signaling in colonic derived macrophages and T-cells. Here we investigated the effect of Lp299v supplement on T1D progression and inflammatory phenotypes in diabetes prone BB DR*lyp/lyp* rats. Rats were weaned at 21 days onto a normal cereal diet (ND) or a gluten-free hydrolyzed casein diet (HCD), with and without daily Lp299v supplementation. All DR*lyp/lyp* ND rats developed T1D by day 83 (mean time to onset of 62.8+/-7.9 days). DR*lyp/lyp* ND+Lp299v rats exhibited an insignificant delay in T1D onset (62.6+/-6.5 days), however 8% remained diabetes-free to day 130. Providing DR*lyp/lyp* rats HCD prevented T1D in 17% of rats (to age 130 days) and significantly delayed onset (mean time to onset 72.8+/-7.3 days, $p<0.001$). Providing DR*lyp/lyp* rats HCD+Lp299v prevented T1D in 25% of rats and more robustly delayed onset (mean time to onset 84.9 +/-14.3 days, $p<0.001$). While multiplex ELISA failed to detect significantly altered plasma cytokine/chemokine levels at 40 days of life, plasma induced transcription revealed the greatest normalization of systemic inflammation in the HCD+Lp299v group. Plasma SCFA levels (propionate and butyrate, $p<0.01$) were elevated in the HCD+Lp299v group compared to the ND group. Global gene expression analysis of pancreatic islets was conducted at 40 days, prior to insulitis. Endoplasmic reticulum (ER) stress has been implicated in the formation of islet neoantigens that may underlie the initial loss of immune tolerance in T1D. Under one or both diets, Lp299v favorably modulated islet expression levels of pathways and transcripts related to inflammation and innate immunity (*Cxcl9, Cxcl10*), oxidative stress (*Gsta1, Gsta4, Gstp1, Gstk1*), as well as ER stress and unfolded protein response (*Cirbp, Edem1, Hspa1a, Atf4*). These ongoing studies add to a growing understanding that inherited susceptibility can be modulated by diet and microbiota.

Pediatric Endocrinology

DIABETES, INSULIN, AND LIPIDS IN PEDIATRIC ENDOCRINOLOGY

Sphingosine 1- Phosphate Lyase Insufficiency Syndrome (SPLIS); A Role in Multiple Endocrinopathies

Ruth Ming Wai Kwong, BMBS, HBSc, MRCPCH, Avinaash Vickram Maharaj, Msc, Louise Metherell, PhD, Rathi Prasad, MBBS, MRCPCH.
William Harvey Research Institute, Queen Mary University of London, London, United Kingdom.

Sphingosine 1-phosphate lyase insufficiency syndrome (SPLIS) was described in 2017 as a novel condition affecting sphingolipid metabolism. There is a multisystemic phenotype including nephrotic syndrome and primary adrenal insufficiency (PAI) and to a lesser extent ichthyosis, neurological disease and lymphopenia. A proportion of patients also presented with hypothyroidism and hypogonadism. To interrogate the endocrine aspect of the syndrome we reviewed clinical data within our patient cohort with SPLIS and those within the wider literature. To date there have been 45 patients identified with SPLIS with significant associated mortality (n=23/45, 51%; 4 of these *in utero*). There is no clear genotype-phenotype correlation. Whilst nephrotic syndrome is most prevalent (n=34/45; 76%), a significant proportion of patients (n=27/45, 60%) also presented with glucocorticoid deficiency, some with additional mineralocorticoid deficiency (n=7/27). Five further patients were noted to have adrenal calcifications though biochemistry was not undertaken. Most patients presented with PAI in the first 2 years of life (n=21/27), with the oldest presentation being 11 years of age. Adrenal calcifications are a common finding in those who had documented imaging (n=13/15, 87%). Primary gonadal failure has been reported in 8 male cases, all with concomitant PAI. Presenting features included microphallus (n=7/8) and cryptorchidism (n=8/8), indicating reduced *in utero* androgen exposure. All who had biochemical evaluation demonstrated raised basal LH and FSH/ exaggerated response to LHRH stimulation, a lack of testosterone response to HCG stimulation and low antimullerian hormone (AMH) levels. To date there are no reports of pubertal delay in female patients, and those of age within our cohort have normal ovarian reserve as evidenced by AMH levels (n=2). Primary hypothyroidism, with mildly raised TSH and low Free T4 is reported in 12 patients. Most did not have goiters and had concomitant PAI and nephrotic syndrome (n=11/12). SPLIS is unique amongst sphingolipid disorders in presenting with significant endocrinopathy. This may be the consequence of the particular sphingolipid signature of the disease and the pathogenic mechanisms need to be explored further. It is clear that endocrine dysfunction needs to be considered at diagnosis and surveillance undertaken to detect evolving disease which could have a significant impact on morbidity and mortality.

Pediatric Endocrinology

DIABETES, INSULIN, AND LIPIDS IN PEDIATRIC ENDOCRINOLOGY

The Effect of Cardiorespiratory Fitness and Insulin Resistance on Bone Health in Hispanic Children

Reem S. Shawar, MD, Maurice Puyau, M.Ed, Roman Shypailo, B.S., Salma Musaad, MD, PhD, Fida F. Bacha, MD.
Baylor College of Medicine, Houston, TX, USA.

Obesity appears to have a negative impact on pediatric bone health, and insulin resistance may mediate this relationship. It is unclear if cardiorespiratory fitness (CRF) has a protective effect on bone in obese children. We tested the hypothesis that CRF attenuates the negative effect of obesity and insulin resistance on skeletal health in a large cohort of Hispanic youth.
We studied 413 (193 males and 220 females) children and adolescents from the Viva la Familia Study. They were all pubertal; mean age (SD) 13.4 ± 2.3 years; 27% were normal weight (NW), 19% overweight (OW) and 54% obese (OB). They underwent measurement of body composition, total body bone mineral content (BMC) and density (BMD) by DXA scan; VO2peak using the ramp protocol on a treadmill for CRF; fasting glucose and insulin. The homeostasis