mouse pituitaries. These findings point to a critical *in vivo* role for Musashi-mediated mRNA translational regulation within the Pou1f1 lineage and specifically in the control of somatotrope maturation and response to metabolic cues.

Diabetes Mellitus and Glucose Metabolism

CLINICAL AND TRANSLATIONAL STUDIES IN DIABETES

Glucokinase Within the Hypothalamic Paraventricular Nucleus Is Important in GLP-1 Release

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When glucose is taken orally more insulin is secreted than when glucose is injected directly into the bloodstream. This is known as the incretin effect. Glucagon like peptide 1 (GLP-1) is one of the hormones responsible for this effect. GLP-1 is released from enteroendocrine L-cells in the gut in response to oral glucose intake. GLP-1 increases insulin synthesis and secretion. Release of GLP-1 is thought to be solely dependent upon gastrointestinal tract mechanisms. Here we identify a brain mechanism via the hypothalamic paraventricular nucleus (PVN) which is important in the release of GLP-1 in response to oral glucose. The role of the paraventricular nucleus in glucose homeostasis was previously unknown. We found that a glucokinase dependent glucose sensing mechanism in the PVN works in conjunction with the gut to regulate GLP-1 release. We show that increasing expression of GK (sense GK, sGK) into the PVN improves glucose tolerance (15 minutes glucose: GFP: 8.93±0.27mmol/L, n=11; sGK: 7.72±0.22mmol/L, n=12; $p<0.01$ and 15 minutes insulin GFP: 2.84±0.14mmol/L, n=11; sGK: 3.73±0.27mmol/L, n=12; $p<0.01$) and increases GLP-1 release in response to oral glucose (GFP: 6.16±0.18mmol/L, n=11; sGK: 6.90±0.26mmol/L, n=12; $p<0.01$). On the contrary decreasing expression of GK (antisense GK, asGK) in the PVN worsens glucose tolerance (30 minutes glucose: GFP: 8.22±0.28mmol/L; asGK: 9.46±0.24mmol/L, n=8; $p<0.01$ and 15 minutes insulin: GFP: 4.07±0.37mmol/L; asGK: 2.25±0.17mmol/L, n=8; $p<0.001$) and blunts (GLP-1 release 30 minutes GLP-1: GFP: 6.93±0.25pMol/L, n=8; $p<0.01$ asGK: 5.47±0.13pMol/L, n=8; $p<0.001$). Our results demonstrate that glucosensitive GK neurones in the PVN, are important to the response to oral glucose and the subsequent release of GLP-1.

Reproductive Endocrinology

BASIC MECHANISMS IN REPRODUCTION: FROM BEGINNING TO END

Placentas from Obese Women Are Resistant to the Effect of Insulin on Triglyceride Content Ex Vivo

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Background: Obesity affects 25% of pregnant women and is associated with a higher risk of neonatal complications, such as macrosomia and increased adiposity. The placenta may contribute to neonatal adiposity by accumulating and transferring excess lipid in response to maternal hyperinsulinemia. We previously found that insulin promotes a 3-fold increase in placental triglyceride (TG) content in lean women. We hypothesized that obese women have higher placental insulin resistance compared to lean women[FC1] with respect to TG content. **Methods**: Healthy, lean women (n=12; mean age 34±1 yrs; BMI 22±0.4 kg/m^2) and non-diabetic, obese women (n=9; mean age 32±2 yrs; BMI 33±0.4 kg/m^2, $p<0.0001$) consented for placenta collection at elective c-section under fasting conditions. Placental villous explants were immediately flash frozen or cultured for 24 hours, starved, then treated for 48 hours with 0.1nM, 1nM, 10nM, or 100nM of insulin, or vehicle. Lipids were extracted from basal and treated explants using a chloroform-methanol separation protocol. TG content was quantified by spectrophotometer and normalized to weight. Data were analyzed by two-way ANOVA. **Results**: Basal placenta tissue from obese women contained a 1.5-fold higher level of TG compared to lean women (9.4±0.5 vs 5.7±0.5 mcg/mg, $p=0.001$). Placental response to insulin in lean women peaked at 1nM insulin (20.2±3.3 mcg/mg), and plateaued at higher doses of 10nM (18.6±3.3 mcg/mg) and 100nM (22.8±2.8 mcg/mg, p=NS respectively). In contrast, placenta explants from obese women required the highest insulin dose of 100 nM for maximal response (23.6±3.2 mcg/mg), and showed a gradual dose response from 0.1 nM insulin (9.5±2), 1nM (14.8±2), 10 nM (16.9±3). At 100nM insulin, the difference in TG content was variable, but on average was 2-fold higher than vehicle treated placenta (vs 11.8±2.5[FC2] [AA3] mcg/mg, $p=0.002$). **Conclusion**: Our findings indicate that placenta from obese women develop insulin resistance similar to peripheral tissues, which can be overcome by high insulin doses. This placental insulin resistance likely occurs in response to chronic hyperinsulinemia, leading to interference of insulin signaling pathways, and may protect the neonate from excessive nutrient flux.

Thyroid

THYROID DISORDERS CASE REPORTS I

Viral-Induced Autoimmune Hyperthyroidism in an Adult Patient Without Established Thyroid Disease

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