

syndrome such as tall stature, hypogonadism, congenital malformations and neurocognitive issues. Hypogonadism may cause abdominal adiposity hence increasing risk of insulin resistance and type 2 diabetes mellitus (DM). Klinefelter syndrome has been associated with certain autoimmune diseases however there is no autoimmune disease link described with XXYY syndrome. We present a patient with XXYY polysomy with insulin requiring DM. **Clinical Case:** A 26-year-old intellectually disabled male with history of XXYY polysomy presented with seizures and was evaluated for DM management. At age 18, he was noted to have hyperglycemia while undergoing dental extractions for brittle enamel leading to the diagnosis of DM. He was initiated on oral medications for a short period of time and transitioned to insulin due to significant hyperglycemia. Endocrine evaluation at the time also revealed hypergonadotropic hypogonadism and evaluation for Klinefelter syndrome revealed 48 XXYY aneuploidy. Patient's history was significant for poorly controlled hyperglycemia with HbA1C ranging in 12–14% range in the last few years. History was negative for diabetic ketoacidosis (DKA) as per his primary endocrinologist, despite being noncompliant with his insulin therapy. History was negative for retinopathy, nephropathy or macrovascular complications, although he did have distal extremity paresthesia. On exam, he was noted to be edentulous with tall stature, BMI 21.7, facial dysmorphism, pes planus and 5th-digit clinodactyly bilaterally. Family history was positive for type 2 DM in father and prediabetes in mother. He presented with seizures and was diagnosed with brain abscess. Hyperglycemia was initially managed with IV insulin, followed by basal/bolus therapy. Fasting labs 20 hours after receiving insulin glargine showed glucose of 284 mg/dL, C-peptide 0.6 ng/mL (ref range: 0.8–3.5), proinsulin less than 1.6 pmol/L (less than 8.0), insulin 4 uIU/mL (3–19) suggestive of type 1 DM. Anti-GAD65 and anti-ICA antibody levels were negative. Additional antibody evaluation for type 1 DM (islet antigen 2, insulin auto-antibody, micro-insulin and zinc transporter 8) is currently pending at the time of writing. **Conclusion:** Prevalence of XXYY syndrome is 1:18 000–1:40 000 in males. There are few case reports describing the association of type 2 DM with this syndrome. Our patient's low BMI, low insulin and C-peptide with hyperglycemia indicate type 1 DM, although the absence of DKA in the setting of noncompliance suggests residual beta cell function or maturity onset diabetes of the young (MODY). Neither T1DM nor MODY has been reported with 48XXYY previously. Clinicians should be aware of this association as it has implications in terms of management of DM.

## Diabetes Mellitus and Glucose Metabolism

### ISLETS AND INSULIN SECRETION

#### *A Novel Population of FOXO1-Expressing Cells in the Stomach Controls Cell Plasticity by Regulating the Cyclin CCNE1*

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A promising new therapy for type 1 diabetes is the reprogramming of gut enteroendocrine cells into cells that produce insulin. The mechanism by which gut epithelial cells are converted into cells that make insulin remains unknown. We have previously found that elimination of Foxo1 in neurogenin3 (Ngn3)-expressing cells of the intestine generates glucose-sensing, insulin-producing cells that are capable of reversing streptozotocin-induced diabetes. Others have reported that stomach cells have a similar property when made to express  $\beta$ -cell factors Ngn3, Pdx1, and MafA. Using mice bearing a Foxo1-GFP knock-in allele, we traced Foxo1-expressing cells in the gut to subpopulations of Ngn3+, as well as acid-secreting parietal stomach cells. To study these cells, we established a 2D co-culture method in which primary stomach cells are isolated from mice and cultured with embryonic fibroblasts. Deletion of Foxo1 in this system generated cells immunoreactive for insulin and C-peptide. Interestingly, Foxo1 ablation also altered the abundance of other gastric cell populations, including more parietal cells and decreased expression of stem cell marker, Lgr5. Tissue-specific elimination of Foxo1 *in vivo* in either Ngn3+ or parietal cells also resulted in the appearance of insulin+ cells, increased parietal cells, and reduced Lgr5 mRNA. To determine how Foxo1 regulated these changes, we used cells isolated from reporter mice that change from red to green after genetic recombination to collect Foxo1-deleted primary stomach cells using FACS. While the mRNA levels of many known Foxo1 targets did not change, cyclin E1 (CCNE1), which regulates G1 to S-phase progression of the cell cycle, was significantly decreased. Conversely, primary stomach cells overexpressing Foxo1 had increased levels of CCNE1. Finally, using ChIP-seq, we found that Foxo1 binds directly to the CCNE1 promoter in a nutrient-dependent manner. In summary, we show that Foxo1 is expressed in a subpopulation of stomach parietal cells and that it regulates their function through the cell cycle regulator, CCNE1.

## Pediatric Endocrinology

### PEDIATRIC ENDOCRINE CASE REPORTS I

#### *Maternal Transmission of Pituitary Stalk Interruption Syndrome (PSIS)*

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**Background:** Pituitary stalk interruption syndrome (PSIS) is a rare entity characterized by thin or absent pituitary stalk, hypoplastic/aplastic anterior pituitary and ectopic posterior pituitary (EPP) on magnetic resonance imaging (MRI). PSIS can be associated with variable degrees of pituitary insufficiency<sup>1</sup>. Most cases of combined pituitary hormone deficiency are sporadic, however in familial cases, there can be AD or AR inheritance with more than 30 genes identified in association with combined pituitary hormone deficiency (CPHD). We describe how diagnosis of 2 children with PSIS led to the discovery of the condition in their mother.