SAT-096
Introduction: Children with isolated (former known as idiopathic) short stature (ISS) have been treated with rhGH or with a variable response. Objectives: To evaluate the short-term response to rhGH therapy in children with ISS with or without a genetic diagnosis. Methods: We analyzed retrospectively the growth rate and height SDS change in the first year of rhGH treatment according to the presence or absence of defects in genes that regulate growth plate. The decision to start rhGH treatment was based on clinical features and the genetic results were obtained during the follow-up. Patients were enrolled in several previous genetic studies using gene candidate approach or multigene sequencing analysis.

Results: A total of 51 prepubertal children (36 boys) with ISS were treated with rhGH. Thirteen of these children started puberty during the treatment and three of them were concomitantly treated with GnRH analog. Basal characteristics of these children were 7.7 ± 3.2 years of age, height SDS -2.5 ± 0.8; sitting height/height (SH/H) SDS 1.2 ± 1.4; BMI SDS 0 ± 1.0 and mild delay of bone age (-1.6 ± 1.3 y). The mean target height was -1.5 ± 0.9y, SH/H (35%) of these children have at least one parent with height SDS < -2 and 3 (6%) both parents are short. Consanguinity was present in 3 (6%) cases. Among this cohort, fifteen children had pathogenic or likely pathogenic allele variants in genes that regulate growth plate: IHH (n = 4), SHOX (n = 9) and NPR2 (n = 2). Seven (47%) of these variants were inherited from a short stature parent. Children with or without an identified genetic cause have similar age and height SDS at the start of the treatment. A higher BMI and SH/H SDS were observed in children with genetic defects than in those without (BMI SDS 0.5 ± 1.1 vs. -0.15 ± 0.9, p = 0.02; SH/H SDS 2.0 ± 1.4 vs. 0.9 ± 1.3, p = 0.006). Additionally, children with genetic defects had a less marked bone age delay (-1.0 ± 1.3 vs. -1.9 ± 1.2; p = 0.02). Both groups were treated with similar rhGH dose (50 μg/kg/day). Patients with and without an identified genetic cause had similar improvement in growth velocity during the first year of therapy: 4.8 ± 1.6 to 8.9 ± 1.7 cm/y for patients with molecular diagnosis vs. 4.6 ± 1.2 to 8.5 ± 2.3 cm/y for those without. This resulted in similar height SDS change during this period for both groups (0.6 ± 0.3 vs. 0.6 ± 0.5 SDS for children with or without a genetic cause, respectively). Age at the start of treatment was the main variable that explains growth response variability during this first year (r² = 0.17, p = 0.009). Conclusion: The presence or absence of an identified genetic cause, involving genes that regulate growth plate, did not significantly influence the short-term growth response to rhGH therapy of children with ISS. Long-term follow-up is still needed to assess the final height of these children and possibly to assess whether there is a different growth rate related to each known affected gene.

Bone and Mineral Metabolism
CLINICAL ASPECTS OF OSTEOPOROSIS AND VITAMIN D ACTION

Implementation of an Osteoporosis Risk Assessment Instrument (ORAI) to Increase Referral Rates for DEXA Scanning in the Primary Care Setting
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MON-391
Abstract
Background/Purpose: Osteoporosis (OP) was first identified and named by healthcare professionals in the 18th century. Today, OP is still the source of fractures which impair mobility, leading to sub-acute stays at rehabilitation centers. A major obstacle is that primary care providers (PCPs) fail to identify warning signs of OP, and inform patients that Dual Energy X-Ray Absorptiometry (DEXA) scans that are one of the best procedures to assess bone health. This project addressed the issue of low rate of referrals for DEXA scans. Theoretical Framework: The Knowledge-to-Action (KTA) model was used to guide this study. Intervention: Implementation of osteoporosis risk assessment instrument. Methods (Design, Sample, Setting, Measures, Analysis): This includes pre-implementation phase, patients’ charts were reviewed; post-implementation phase, the number of people referred to have DEXA scans were analyzed; the evaluation phase, results compared to the previous data. The project focus exclusively on women and men ages 50 to 89 years in two primary care offices in New Jersey. Descriptive analyses concentrated on whether or not ORAI was the tool to increase DEXA scans. Results: The data analysis reflected that the baseline referral rates increased from 1.3 % to 42 % and patients who scored high on the risk assessment instrument have been referred more often than not. Moreover, patients who are at risk and younger than 65 years of age, risk assessment tools led to a positive referral for a DEXA scan. Those who are older than 65 years, risk assessment tools like ORAI should be given with fracture risk assessment tools. This is especially the case when dealing with men, a demographic group often overlooked in the fight against OP. Conclusions Implications: If this project is to be applied at other clinics, more and more patients would be referred, raising awareness of the medical benefits of early detection. Reasonably, covering a broader section of patients, earlier in their lives, will increase clinical income, bringing more patients to primary care offices.

Adipose Tissue, Appetite, and Obesity
ADIPOSE TISSUE BIOLOGY AND OBESITY
Uc.336-As Inhibits White Adipocyte Differentiation and Promotes White to Brown Conversion
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SAT-584
Brown adipose tissue (BAT) has gained its popularity since it shows great potential in counteracting obesity and metabolic diseases development. Transcribed ultraconserved regions (T-UCRs), a novel class of long non-coding RNA (lncRNAs), have been implicated in regulating diverse biological processes, including the process of white fat browning. However, the functional and mechanistic details of T-UCRs in the browning process are poorly understood. Here, we identified that a T-UCR, uc.336-as, played an
important role during the browning process. uc.336-as was significantly elevated during browning process induced by exendin-4 or β3-adrenergic agonist (CL316,243). Moreover, we found that uc.336-as promoted browning process and inhibited adipogenesis. Finally, we identified that uc.336-as promoted the expression of browning-related genes via influencing the p38 mitogen-activated protein kinase (p38 MAPK) signaling, an essential signal pathway in metabolism. Taken together, our data show that uc.336-as acts as a negative regulator in white adipocyte differentiation and promotes the browning process, suggesting a potential therapeutic role for uc.336-as in controlling obesity.

Pediatric Endocrinology
PEDIATRIC ENDOCRINE CASE REPORTS II
17B-hydroxysteroid dehydrogenase Type 3 Deficiency: An Under-Recognized Cause of 46,XY DSD in the United States?
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MON-066
Title: 17β-hydroxysteroid dehydrogenase type 3 deficiency: An under-recognized cause of 46,XY DSD in the United States?
Introduction: The 17β-hydroxysteroid dehydrogenase type 3 (17BHSD3) enzyme, expressed in the testes, converts androstenedione (A) to testosterone (T). 17BHSD3 deficiency causes a 46,XY difference of sex development (DSD), or intersex condition, characterized by lack of prenatal virilization followed by marked virilization at puberty due to peripheral conversion of A to T by other 17BHSD isoenzymes. Diagnosis is suspected with an abnormal T:A ratio of <0.8 and confirmed by HSD17B3 sequencing and deletion/duplication analysis. 17BHSD3 deficiency may present similarly to complete or partial androgen insensitivity syndrome (CAIS, PAIS) due to undervirilization in infancy, and to 5α-reductase deficiency due to virilization during puberty. Previously, only 12 cases of this autosomal recessive disorder have been reported in the US. We report 3 cases of 17BHSD3 deficiency diagnosed at a single pediatric center in the US.
Clinical Cases: Patient A had atypical genitalia at birth and a presumed diagnosis of PAIS though sequencing of AR was normal. He underwent multiple genital surgeries throughout childhood, had significant psychiatric and behavioral concerns, and was referred to our multidisciplinary clinic at age 16 years. Additional diagnostic testing revealed a T:A ratio of 0.29 consistent with 17BHSD3 deficiency; confirmatory genetic testing was deferred per family preference.
Patient B was noted to have testicular tissue present at age 3 years during an inguinal hernia repair and was diagnosed with CAIS. She presented to our institution at age 14 years with clitoromegaly. T:A ratio was 0.29 and genetic testing revealed a pathogenic splice site variant in HSD17B3. She requested gonadectomy due to unwanted virilization inconsistent with her female gender identity.

Following gonadectomy at age 16 years, she began estrogen treatment and vaginal dilations. Patient C presented to our institution at age 18 years with pubertal delay and primary amenorrhea. She was noted to have palpable gonads and clitoromegaly. Evaluation revealed a 46,XY karyotype and a T:A ratio of 0.32. She was raised as a girl and identified as female. She requested gonadectomy to avoid further virilization, after which she began estrogen for pubertal induction. She deferred confirmatory genetic testing.
Conclusions: Previous studies noted 17BHSD3 deficiency to be rare in the US, but the presence of 2 suspected and 1 confirmed diagnoses at a single US institution suggests it is likely more common and may be misdiagnosed as other types of DSD. Differentiating 17BHSD3 deficiency from other causes of 46,XY DSD is essential to inform accurate counseling about sex designation, gender identity, gonadal function, malignancy risk, potential fertility and heritability.

Bone and Mineral Metabolism
BONE DISEASE FROM BENCH TO BEDSIDE
Glucagon-like Peptide 1 (GLP-1) Acts Directly On Human Osteoclasts To Increase Differentiation And Bone Resorptive Activity
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SUN-347
Glucagon-like peptide 1 (GLP-1) is an intestinal hormone released in response to nutrient intake that promotes glucose-dependent insulin secretion by acting upon the pancreatic GLP-1 receptor (GLP-1R). GLP-1R agonists (GLP-1RAs) are widely used in treatment of type 2 diabetics. Preclinical data indicate that GLP-1RAs could be repurposed to treat low bone mass as GLP-1R-depleted mice have higher bone resorption and thinner cortical bones, while insulinopenic and insulin resistant rats have improved bone formation and reduced bone mass deterioration when treated with GLP-1 or GLP-1RAs. However, the effect of GLP-1 and GLP-1RAs on human bone cells remains undetermined. We aimed to elucidate the effect of GLP-1 on primary human osteoclast (OC) and osteoblast (OB) cultures. OCs were differentiated over 10 days from human blood-derived CD14+ monocytes and OBs over 4–6 weeks from human bone. Cells were seeded on bovine bone slices. GLP-1 increased the eroded bone surface percentage compared to vehicle in both OC monocultures (1nM P=0.002; 10nM P=0.023; n=8 donors) and OC+OB co-cultures (1nM P=0.013; 10nM P=0.012; n=8 donors). We then tested the effects of GLP-1 on osteoblast activity in OC+OB co-cultures by measuring alkaline phosphatase (ALP). We found that GLP-1 increased ALP in OC+OB cultures (1nM, P=0.049; 10nM, P=0.019) and these effects were reversed by the GLP-1R