of TS was based on recommendations by clinical practice guidelines from 2016 Cincinnati International TS meeting. Peripheral venous sample was collected in EDTA tubes and DNA was extracted using Qiagen-DNAeasy Blood and Tissue kit (Cat No. 69504). DNA samples were then hybridized to the Affymetrix CytoScan 750K array as per manufacturer's instructions. The data obtained was analysed using Chromosomal Analysis suite software and public genomic databases- ISCA, OMIM, DGV, DECIPHER. For bioinformatic analysis, all the genes (172) implicated in TS were retrieved from DisGeNET database. A TS-interactome of 4033 genes was then constructed from these genes and their first-degree neighbours from complete human interactome. Thereafter compilation was done based on CMA results and a protein-protein interaction network of 316 nodes was constructed. **Results:** Mean age of study cohort was 15.8 ± 3.64 years with short stature being the most common presenting phenotype (91.4%). CMA analysis detected copy number variations (CNVs) on chromosome 14 in 42 (89.3%) of 47 cases while X chromosome CNVs were present in only 28 (59.5%) cases, with all patients clinically qualifying as TS. Total 445 CNVs were discovered on X chromosome and 64 CNVs were found on Chromosome 14 exhibiting either CNV gain at 14q32.33 or CNV loss at 14q11.2 or both. The 30 cell karyotype was available for 27 patients and was found to be false negative in 7 (14.8%) patients. Also, 6 out of 47 cases had Y chromosome translocation detected on CMA that failed detection by karyotype. On enrichment analysis, thirty KEGG pathways were found to be enriched by the overlapping genes between TS-interactome and the interactome constructed by genes located within 14q11.2, and 14q32.33 67% of genes (212) in this network overlap with TS-interactome.
Conclusions: CMA is a superior diagnostic modality for TS than karyotyping. Functional interactomes between Chromosome X and Chromosome 14 on enrichment analysis reveal novel pathways underlying phenotypic manifestations.

Reproductive Endocrinology

TRANSGENDER, DSD, AND TURNER SYNDROME

Development of Repository From a Pediatric Gender Clinic

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Objectives: With the publication of updated guidelines for care of transgender and gender non-conforming individuals, there has been an increase in the presence of gender diversity in both mainstream media and medical literature. Several gaps currently exist in medical knowledge regarding long term effects of gender-affirming therapies. There is a lack of standardization in study design, patient sampling, and outcome measures, and most studies are retrospective. Here we describe the creation of both a retrospective and prospective repository of patients who presented to the Massachusetts Medical School-Baystate Medical Center (UMass-Baystate) pediatric gender program.
Methods: Baystate Medical Center is located in western MA and is a tertiary referral center. A pediatric gender clinic was created in 2014. A repository containing both retrospective and prospective data was approved by the UMass-Baystate IRB to include patients ages 2 to 24 years of age who presented to our gender clinic. Retrospective data was obtained using the McKesson billing database. Sociodemographic, clinical and behavioral health data were collected. We are consenting individuals as they present to the clinic for the prospective component. Those that have consented fill out a survey at each visit. The repository has been approved to follow outcome data for 25 years.
Results: To date, we have 218 individuals in the repository, 75 of which are in the prospective component. Age of presentation ranged from 6 yrs to 24 yrs with an average age of 15 yrs. 62% identified as transmale, 31% as transfemale and the remainder as gender fluid or other. 75% have been prescribed gender affirming hormone therapy (56% GnRH agonist therapy, 20% estrogen, 58% testosterone). Of those being followed prospectively, 76% identified as white, 19% Hispanic. 79% were satisfied or very satisfied with their care.
Conclusions: Here we describe the demographic and clinical characteristics of patients that have presented to our gender clinic since 2014. The creation of our gender repository will allow us to assess sociodemographic, clinical and behavioral health outcomes of treatment, including metabolic parameters, bone health, and mental health outcomes in our pediatric population. Future projects include assessment of the change in cardiovascular risk in individuals on gender-affirming hormone therapy.

Reproductive Endocrinology

TRANSGENDER, DSD, AND TURNER SYNDROME

Evaluation of Enzymatic Activity of Various HSD17B3 Mutants Using Androgen Receptor-Mediated Transactivation

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17β-Hydroxysteroid dehydrogenases (17β-HSDs, HSD17B) catalyze the reduction of 17-ketosteroids and the oxidation of 17β-hydroxysteroids to regulate the production of sex steroids. Among HSD17B family, 17β-HSD type 3 (HSD17B3) is expressed in testicular Leydig cells and contributes to development of male sexual characteristics by converting androstenedione (A4) to testosterone (T). Mutations of HSD17B3 genes cause a 46,XY disorder of sexual development (46,XY DSD) as a result of low T production. Therefore, the evaluation of HSD17B3 enzymatic activity is important for understanding and diagnosing this disorder. Although various amino acid substitutions of HSD17B3 have been reported in previous studies, the enzymatic activities of these proteins were often not defined. This is probably due to the difficulties that such enzymatic activities have been evaluated by quantifying the conversion of A4 into T using radioactive isotopes and liquid chromatography-mass spectrometry-mass spectrometry (LC-MS/MS). We adapted a method that easily evaluates enzymatic activity of HSD17B3 proteins by quantifying the conversion from A4 to T using androgen

receptor (AR)-mediated transactivation. HEK293 cells were transfected to express human HSD17B3, and incubated medium containing A4. Depending on the incubation time with HSD17B3-expressing cells, the culture media progressively increased luciferase activities in CV-1 cells, transfected with the AR expression vector and androgen-responsive reporter. These luciferase activities reflected T concentrations in culture media defined by LC-MS/MS. This system is also applicable to detect the conversion of A4 to T by HSD17B1 and HSD17B5. In addition, it can evaluate the conversion of 11-ketoandrostenedione to 11-ketotestosterone by HSD17B family. Establishment of HEK293 cells expressing various missense mutations in the HSD17B3 gene with (N74T, A188V, M197K, A200V,, V225M, H271R) or without (V31I, E67K and G289S) the manifestation of 46,XY DSD revealed that this system is effective to evaluate the enzymatic activities of mutant proteins. A188V, A200V, V225M and H271R mutations completely inactivated the enzymatic function. N74T and M197K mutations showed some residual activities. In contrast, V31I, E67K and G289S substitutions showed similar activities as the wild-type protein.

Reproductive Endocrinology

TRANSGENDER, DSD, AND TURNER SYNDROME

Evaluation of Turner Syndrome International Consensus Guideline Compliance in Multiple Subspecialty Clinics Verses a Coordinated Multidisciplinary Clinic Format.

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Turner syndrome's (TS) lifelong association with multi-organ system comorbidities necessitates the effective implementation of, and adherence to, screening guidelines. Our team evaluated the effectiveness in implementing the 2016 Cincinnati International Turner Syndrome consensus guidelines [1] in a single, coordinated, multidisciplinary clinic (MDC) day format compared to multiple separate subspecialty clinic visits. A retrospective analysis of patients with TS followed at our pediatric tertiary referral center between December 2016 and April 2020 was conducted. Exclusion criteria included patients that were not seen in our pediatric endocrine clinic for over 24 months, age over 22 years, and those without confirmed genetic diagnosis of TS. The population was separated into two groups; girls who attended at least 1 MDC day each year and girls who had at least 1 endocrinology clinic visit in the last 14 months, but who were not part of the MDC (non-MDC). Age appropriate screenings included TSH, hepatic function test, Vitamin D level, blood glucose and/or HgA1C, celiac screening panel, hearing/auditory screening, eye examination, electrocardiogram, and echocardiogram. A total of 112 girls met study criteria. Sixty-eight were managed in the MDC and 44 managed in non-MDC. Only 36.6% of all the girls met all the above age-appropriate screening recommendations, 75.6% of which were managed in MDC (p-value 0.014). MDC girls had higher screening compliance rates vs non-MDC girls for TSH (95% vs 76%, p-value 0.017), auditory evaluation (85% vs 50%, p-value <0.001), HgA1c and/or serum blood glucose levels (97% vs 76%, p-value 0.017), and tissue transglutaminase levels (95% vs 83%, p-value 0.048). No statistically significant difference was found with overall screening guideline compliance and insurance status, race/ethnicity, or age at time of the patients last recorded clinic visit. In conclusion, the MDC day format showed superior screening guideline compliance, both overall and to multiple specific screening tests, compared to those seen in multiple uncoordinated, single-disciplinary individual provider clinics. Overall guideline adherence remained low (36.6%), highlighting the need for continued optimization and improvement in guideline compliance. **Reference**: [1] Gravholt, C.H., et al., Eur J Endocrinol, 2017. 177(3): p. G1-G70.

Reproductive Endocrinology

TRANSGENDER, DSD, AND TURNER SYNDROME

Hepatic Abnormalities in Youth With Turner Syndrome

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Background: While cardiac complications, short stature, and infertility are often discussed in the context of Turner Syndrome (TS), abnormalities of liver function are less well described. In order to address this gap in knowledge, we sought to better characterize hepatic abnormalities in youth with TS. **Methods:** PEDSnet is a collaboration across 7 major US pediatric institutions that unifies electronic medical data including diagnoses, prescriptions, and laboratory measurements for over 6 million children. 2,145 females with a diagnosis of TS were matched to 8,580 females without TS (1:4 ratio) on site, race (68% White), ethnicity (15% Hispanic), payer source, year of birth, age at most recent visit (median 14 years), and duration of care (mean 8 years). Outcomes of interest included highest recorded liver enzyme values (AST and ALT) categorized as normal or above the upper limit of normal (ULN) defined as >95th percentile for their age, and specific liver diagnoses. Proportions were compared between the cohorts using odds ratios (OR) and 95% confidence intervals (CI) from a generalized estimating equations approach. Multinomial logistic regression was conducted to investigate potential risk factors for liver abnormalities within the TS cohort. **Results:** Out of 1,159 girls with TS who had liver enzymes recorded in PEDSnet, 58% had at least one AST or ALT above the ULN. TS patients were more likely to have enzymes 1-2 times ULN (OR: 1.7, 95% CI: 1.4-1.9), more likely to be in the 2-3 times ULN category (OR: 2.7, 95% CI: 1.7-3.3), and more likely to be in the >3 times ULN category (OR: 1.7, 95% CI: 1.3-2.2) compared to girls without TS. TS patients were also more likely to have any liver diagnosis (OR: 2.4, 95% CI: 1.7-3.3), including significantly higher risk of fatty liver disease (OR: 1.9, 95% CI: 1.1-3.2), hepatitis (OR: 3.7, 95% CI: 1.9-7.1), cirrhosis/fibrosis (OR: