increase resulting in androgen excess in both salt-wasting (SW) or simple virilizing (SV) forms. As androgens play a role in the human psychosexual development favoring male psychosexuality, this study was designed to evaluate the impact of androgen exposure on the psychosexuality of individuals with CAH due 21-hydroxylase deficiency. **Methods:** This retrospective cohort includes 46,XX individuals (115 female-assigned; 8 male-assigned) with a molecular diagnosis of CAH due to *CYP21A2* pathogenic variants in homozygous or compounds heterozygous state. External genitalia virilization was scored using Prader scale. Phenotype, time at diagnosis, sex assignment, and gender change were assessed. The gender role at childhood was assessed through the playmates and toys profile at childhood. Gender identity was assessed by a projective psychological test (HTP). Sexual orientation was assessed by self-report sexual identity. Compliance of glucocorticoid replacement was assessed by adequate testosterone and androstenedione serum levels for age. **Results:** CAH was diagnosed at the neonatal time in 73% (n=78). Fifth-nine (51%) had the SW form and 49% (n=56) had the SV form. While all cases of SW were diagnosed at the neonatal time (0.12 ± 0.14 months), the mean age at diagnosis among SV was 6.03 ± 8.45 years (p=<.001). The median of Prader score was 3 in both forms. Male sex assignment was associated with more virilized external genitalia (p=.002). Gender change occurred in 6 cases (female to male), all with SV form. The prader score was higher among those who changed gender (p=.01). All of those who changed their gender had poor treatment compliance. A total of 13% (n=15) of all groups defined themselves as homosexual. There was a strong association between male toys and preference for male playmates in childhood with homosexuality and male gender identity in adulthood with both gender change from female to male and homosexuality. **Conclusion:** Prenatal androgen exposure favors male psychosexuality in 46,XX CAH individuals as observed by the association between highest Prader scores and all assessed psychosexual outcomes. This influence is also substantiated by post-natal androgen exposure as observed by compliance issues and late diagnosis among those who changed from female to male gender.

Genetics and Development (including Gene Regulation)

FROM BENCH TO BEDSIDE: GENETICS, DEVELOPMENT AND CELL SIGNALING IN ENDOCRINOLOGY

Electronic Health Record-Based Genome-Wide Meta-Analysis Identifies New Susceptibility Loci for Non-Alcoholic Fatty Liver Disease

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Background: Non-alcoholic fatty liver disease (NAFLD) is the most prevalent form of liver disease. Observational studies documented associations of NAFLD with several chronic and infectious diseases but whether these associations underlie causal effects is unknown. The molecular mechanisms and genetic architecture of NAFLD are poorly understood. Our objectives were to identify genetic loci associated with NAFLD and determine whether the presence of NAFLD was causally associated with human diseases.

Methods: We created a NAFLD genetic instrument through the identification of independent single-nucleotide polymorphisms (SNPs) associated with NAFLD in a meta-analysis of genome-wide association study (GWAS) (6715 cases and 682,748 controls). Using inverse-variance weighted Mendelian Randomization (MR), we investigated the impact of NAFLD on human disease-related phenotypes in the UK Biobank and FinnGen cohorts as well as in the COVID-19 host genetics initiative. **Results:** We first performed a GWAS meta-analysis of four cohorts and found variants significantly associated with NAFLD (p<5.0E-8) at six genetic loci (*MTARC1*, *GCKR*, *TRIB1*, *LMO3*, *SUGP1* [*TM6SF2*] and *PNPLA3*). Using a risk factor informed Bayesian approach (bGWAS), we identify variants at three additional loci (*LPL*, *FTO*, and *APOE*). To determine if the association between NAFLD and human diseases shows evidence of causality, we performed MR across the human disease-related phenome (>800 diseases) using a genetic instrument for NAFLD. Results of these analyses suggest that NAFLD was not causally associated with diseases outside the spectrum of liver diseases. We also found no causal association between genetically predicted NAFLD and COVID-19-related outcomes.

Conclusions: This study identified several new genetic loci associated with NAFLD. NAFLD was not causally associated with diseases outside those of the spectrum of liver diseases. This finding suggests that the resolution of NAFLD might not prevent other diseases previously associated with NAFLD.

Genetics and Development (including Gene Regulation)

FROM BENCH TO BEDSIDE: GENETICS, DEVELOPMENT AND CELL SIGNALING IN ENDOCRINOLOGY

Evaluation of Mayer-Rokitansky-Kuster-Hauser (MRKH) Patient Families by Whole Genome Sequencing

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Introduction: MRKH is a characterized by the congenital absence of the uterus and vagina in 46,XX individuals.