2019 Young Investigator Award 1st Runner-Up

620: Expression and sequencing of genes involved in the pathogenesis of Mayer Rokitansky Kuster Hauser syndrome

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Objective
Uterine and vaginal anomalies occur commonly in women with reproductive dysfunction. Mayer Rokitansky Kuster Hauser syndrome (MRKH), otherwise known as Mullerian Aplasia, falls at the severe end of the spectrum of such anomalies and affects approximately 1 in every 4000 women. This syndrome manifests itself as the absence of the uterus and/or vagina and may be associated with other anomalies such as kidney, heart, or bone defects. Although a genetic component to MRKH has been suggested, little is known of causative genes. The purpose of this study was to investigate candidate genes and gain a further understanding of the pathogenesis of MRKH and associated anomalies.
Design
This study utilized a cross-sectional approach to examine the genetic framework of a selection of patients currently diagnosed with MRKH as well as relevant family members.
Materials and Methods
The candidate genes being analyzed either came from a list of gene variants stratified during whole exome sequencing (WES) on 14 MRKH trios (1 MRKH proband + 2 family members), 2 duos, and 1 singlet or from close vicinity to breakpoints identified on a balanced chromosomal translocation (3;16) within an MRKH patient. Sanger sequencing was used to confirm likely pathogenic gene variants from WES. Reverse transcriptase-PCR (RT-PCR) was used to test the expression of all 38 genes in MRKH related organ tissue (kidney, heart, and uterus).
Results
DNA Sequencing of variants resulted in 15 of the 17 variants being confirmed, with one unconfirmed, and one in progress. Findings from RT-PCR resulted in 26 of 38 genes showing expression in >1 MRKH dependent tissue with 9 of the other genes still in progress.
Conclusions
Our findings have permitted prioritization of candidate genes that will be considered for sequencing on a larger sample of MRKH patients. Likely pathogenic variants with detrimental effects in vitro that segregate with the phenotype will suggest a role in the pathogenesis of MRKH.
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Disclosure
None