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Whole exome sequencing analysis identifies OCRL variant in child diagnosed with ROHHAD syndrome

Introduction: Rapid-onset obesity with hypothalamic dysfunction, hypoventilation, and autonomic dysregulation (ROHHAD) is a rare disorder named based on its clinical characteristics. The disease, which typically presents in the first few years of life, has been described in literature in only about 150 cases. The cause of the disorder is unknown, so this study seeks to use whole exome sequencing (WES) analysis to determine a genetic basis for ROHHAD in a specific patient. WES is a process that determines the entire nucleotide sequence of all exons in a human's genome.
Methods: This study analyzed the WES results in a 4-year-old male diagnosed with ROHHAD and his healthy parents. WES was done following DNA extraction. All variants were found and uploaded to seqr, a software tool where variants could be filtered based on relevance for being pathogenic for a rare disease. To determine their potential to be causal for ROHHAD, the resulting variants were studied using a review of literature and public data on the variants and the genes they are on.
Results: From the patient's original set of thousands of variants that were filtered on seqr, there were 14 resulting variants on 10 distinct genes that fit the study's criteria to be possibly disease-causing. Further examination yielded one rare frameshift variant on the OCRL gene with the potential to be pathogenic for our patient's ROHHAD. OCRL is an X-linked gene that plays a role in delivery of materials to the primary cilium of a cell, a location that is dysfunctional in other obesity related syndromes. Also, OCRL mutations underlie two rare diseases, Lowe Disease and Dent Disease, which present with a range of symptoms that overlap those of ROHHAD in this patient.
Conclusions: This study identified a genetic variant that is a strong candidate for being associated with this patient's ROHHAD phenotype. Identifying novel genetic variants provides a better understanding of ROHHAD and other rare diseases.

Additional contributors to this project:
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