Molecular diagnostic yield of combined CNV and next generation sequencing in subjects with autism spectrum disorder

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Autism spectrum disorder (ASD) is a neurodevelopmental disorder with substantial genetic and phenotypic diversity. Structural alterations such as chromosomal abnormalities and copy number variations (CNVs) were the first culprits of ASD, however, they account for a small portion of the total cases. After the emergence of next-generation sequencing, the focus has shifted towards investigating the role of inherited and de novo point mutations using whole genome or whole exome approaches. The steep price drop and improved speed of whole exome sequencing (WES) have made this technology increasingly available as a diagnostic tool for patients with complex neurodevelopmental disorders. However, the clinical utility of WES in ASD is generally understudied and is yet to be determined in consanguineous populations. We describe here a comprehensive molecular analysis pipeline that could enable clinicians to establish molecular diagnosis with more confidence and has the potential to better inform genetic counseling. The study was performed on 135 individuals with confirmed diagnosis of ASD from 23 multiplexes and 81 simplex Saudi families. All samples were subjected to two step molecular evaluation. First, CNV analysis using the Affymetrix Cytoscan HD followed by next-generation sequencing using a customized gene-panel comprising 232 ASD associated genes developed by the Saudi Human Genome project team. Also, WES was carried out in a subset of samples in which no candidate variants were identified by the two former approaches. Disordered sleep, chronic headache, and decreased cognitive processing speed are common and often untreatable manifestations of traumatic brain injury that can devastate an individual's quality of life. Our results demonstrate the recoverability of chronic symptoms beyond what was previously thought possible? These findings have important applications in the fields of applied neuroscience and rehabilitation.

Speaker Biography

Bashayer Al-Mubarak, PhD, Post-doctoral Research Fellow in the Behavioral Genetics Unit part of the Department of Genetics at King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia. She has completed her PhD in Neurobiology at the University of Edinburgh, which was focused on studying the transcriptional regulation of anti-oxidant defenses in neuronal and glial cells. Soon after obtaining her degree, she did her first Post-doctoral Fellowship with Dr. Alexander Jeans at the Department of Physiology Anatomy and Genetics (DPAG) in the University of Oxford, where she worked on investigating the role of presynaptic voltage-gated calcium channels in regulating a phenomenon known as "homeostatic synaptic plasticity" (an endogenous regulatory mechanism that maintains neuronal activity with normal levels) in hippocampal neurons. After completing her post at DPAG, she has joined the Behavioral Genetics Unit and has been working since then, on the genetic basis of neurodegenerative and neurodevelopmental diseases such as Parkinson's, Autism and Attention Deficit Hyperactivity Disorder.

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