Abstract Title: Deciphering genetic architecture of autism spectrum disorders in India using short and long read sequencing technologies

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Abstract: Autism spectrum disorder (ASD) is a heterogeneous group of neurodevelopmental disorders (NDD) and is characterized by impaired social communication along with repetitive behavior or restricted interests which can persist throughout lifetime. Guidelines put forth a decade ago by the American College of Medical Genetics suggests using chromosomal microarray (CMA) as a first line test for genetic diagnosis of ASD. However, latest results from whole exome sequencing (WES) studies suggests higher diagnostic yield compared to CMA due to detection of de novo SNVs; a significant cause for NDD. No study has been performed to delineate the genetic architecture of ASD in the Indian population which can help in selection of first-tier test. I will present results of the first systematic study to assess the genetic architecture and diagnostic yields of karyotype, Fragile-X testing, CMA and WES in a cohort of 101 patient-parent trios with ASD from India. I will show a significant improvement in diagnostic yield by WES compared to CMA and a significant genetic burden conferred by de novo SNVs involved in synaptic formation, transcription and its regulation, ubiquitination and chromatin remodeling. I will also present ASD cases where complex structural variants, which were missed by WES and CMA, are detected by third generation, low-pass, whole genome sequencing technology- specifically- Oxford Nanopore. This is leading to new insights into the genetic diversity underlying ASD which will help guide future of genetic and therapeutic research.

Area of expertise: Autism spectrum disorder, structural variation, second and third sequencing, computational biology, hereditary cancer prevention, male infertility, lysosomal storage disorders