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Abstract Topic:- Clinical Genetics

Abstract Title:- Whole Genome Sequencing Improves the Diagnosis of Neuromuscular Disorders

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Aims:-Whole-genome sequencing

(WGS) evaluates the diagnostic yield and workflow of genome-scale sequencing in patients with neuromuscular disorders (NMDs).

Methods:- The blood samples were sent to the Neuberg Center for Genomic Medicine for whole genome sequencing and whole exome sequencing. Isolated the genomic DNA and prepared the libraries as per the protocol. Prepared libraries were sequenced by PE150 chemistry. The data from each sample is mapped to the human reference genome (GRCh38). Variant quality score recalibration method, which uses machine learning to identify annotation profiles of variants to get high-confident variant calls In order to decrease the noise of sequencing data, data filtering is used to remove reads containing sequencing adapters and reads with a low-quality base ratio. The bioinformatics tools were used to perform gene-based annotation and filter-based annotation. The American College of Medical Genetics and Genomics (ACMG) and the Association for Molecular Pathology (AMP) guidelines are used for variant classification.

Results:- We compared whole-exome sequencing (WES) and whole-genome sequencing (WGS), whose whole-exome results were negative, but the clinically diagnosed phenotype was present for neuromuscular disorders in patients. For both SNVs and indels, the distributions of coverage depth, genotype quality, and minor read ratio were more uniform for WGS than WES. We Sanger-sequenced a random selection of these exclusive variants. For SNVs, the proportion of false-positive variants was higher for WES than WGS. For indels, the proportions of false-positive variants were similar for WES and WGS. WES was not reliable for the detection of CNV and was unable to identify simple sequence repeat (SSR) variations. WGS is currently more expensive than WES, but its cost should decrease more rapidly than that of WES. WGS is more efficient than WES for detecting mutations in the targeted exome.

Conclusions:- Our findings confirm that WGS provides a much more uniform distribution of sequencing quality than WES. So, it improves the diagnosis of neuromuscular disorders in patients.

Keywords:- neuromuscular disorders, whole genome sequencing, next-generation sequencing, whole exome sequencing