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Identification of a novel mutation in Mitochondrial DNA depletion syndrome type5 by Whole Exome Sequencing

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Introduction

Mitochondrial DNA depletion syndrome type5 is a genetically and clinically heterogeneous disorder with autosomal recessive inheritance. It is characterized by infantile onset of hypotonia, progressive neurologic deterioration, and hyperkinetic-dystonic movement disorder. This study presents a patient with no definite clinical diagnosis. WES (Whole Exome Sequencing) revealed a novel mutation.

Materials and Method

The patient is a 7-year-old boy from a consanguineous family. He suffered from poor feeding in infancy, metabolic acidosis, severe irritability and developmental delay.

WES was requested. Sanger sequencing was used for segregation analysis of the identified variant. Insillico analysis of the newly identified variant was done.

Results

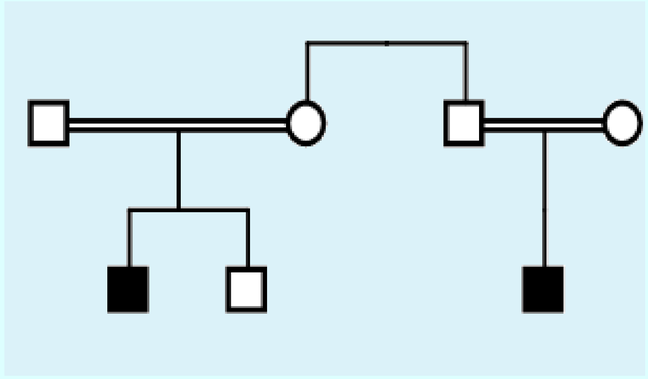
Clinical features and initial laboratory findings were in favor of a metabolic disease but further studies ruled out metabolic diseases. Further analysis revealed elevated concentration of succinylcarnitine in blood that is compatible with mitochondrial disorder. The pattern of organic acids in urine is normal. Abnormal EEG, EMG-NCV consistent with congenital myopathy

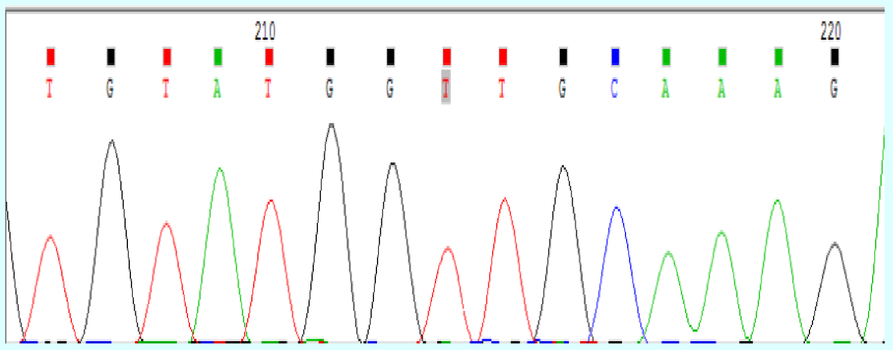
WES revealed a previously unreported homozygous variant in the SUCLA2 gene.

Discussion

The mutation caused substitution of Aspartic acid (negative charge) to valine which is a non-polar residue. The mutation will effect on protein structure and probably function. All Insilico analysis supported the pathogenicity of the mutation. This mutation is compatible with Mitochondrial DNA depletion syndrome type5 .No other phenotypes are known to be associated with pathogenic variants in SUCLA2.

Exome sequencing is a powerful technique for identifying the causative mutations especially in patients with no definite clinical diagnosis





Keywords: Mitochondrial DNA depletion syndrome type5, SUCLA2 gene, Whole exome sequencing.