P-043 - A Novel Candidate Frameshift Mutation For Leigh Syndrome

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Leigh syndrome (LS) is progressive neurodegenerative mitochondrial disorder which is characterized by focal, symmetrical, and necrotic lesions in the thalamus, the brain stem and the columns of the spinal cord. SURF1 gene, one of the genes responsible for Leigh syndrome, is located at chromosome 9p34 which encodes a protein localized to the inner mitochondrial membrane. This protein is involved in the biogenesis of cytochrome c oxidase complex. A couple who have consanguinity between them have been admitted to our department due to the fact that they have 3 children who died with the suspicion of mitochondrial disease. Their two children died at the age of 3 and one at the age of 9. Children had similar findings such as difficulty swallowing, tremor, hypotonia, difficulty breathing and severe psychomotor retardation. Mitochondrial genome analysis of one of them was normal. We planned the Whole-Exome Sequencing for the detection of common heterozygous variants. In both father and mother, we identified a novel heterozygous deletion in SURF1 (NM_003172.3) gene c.252delG which is not found in clinical databases such as ClinVar or Human Genome Database (HGMD). According to American College of Medical Genetics (ACMG) criteria (PVS1, PM2, PP3) it is classified as 'pathogenic'. We also determined the same variant as homozygous in their passed away child with Sanger sequencing. With this mutation, we added a new one to the variants detected in the SURF1 gene. Functional studies are needed to contribute to the determination of the pathogenicity of this variant.

KEYWORDS: Leigh syndrome, c.252delG, SURF1 gene, Whole Exom Sequencing

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ABSTRACT BOOK

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