OP 04 - Identification of mitochondrial mutations associated with rare undiagnosed disease phenotypes in Sri Lanka

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Introduction: Mitochondrial disorders are a clinically heterogeneous group of diseases with an overlapping range of disease phenotypes with an estimated prevalence of 1 in 5000. This project aims to identify disease causing variants present in mitochondrial DNA and establish a foundational database of mitochondrial genetic variants in Sri Lanka. The study was designed to identify contributing mitochondrial genetic variants in patients with rare and undiagnosed genetic diseases. This is a case series, done in follow-up of a previous study conducted at the Human Genetics Unit, FOM, UOC.

Methods: Ten patients with rare and undiagnosed genetic diseases were used for this study with informed consent obtained for such studies. The mtDNA was extracted using the QIAGEN Blood DNA Mini Kit. MT-ND1 gene region of the mtDNA genome was amplified using Polymerase Chain Reaction (PCR). Sanger sequencing was performed to identify and confirm the mtDNA variants. Base calling was performed using Codon Code Aligner tool and novel variants were identified and examined using public databases. Phenotypic correlations were done to compare clinical symptoms with variants in each sample.

Results: Variants in the MT-ND1 gene associated with adult onset dystonia, mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke- like episodes (MELAS), Leber hereditary optic neuropathy (LHON), Leber optic atrophy as well as Noonan's syndrome were identified. 2 of the 3 sequenced samples had mtDNA variants showing phenotypic correlation with patient symptoms.

Conclusion: These cases showed variants which were likely to be pathogenic according to population databases. This helped to arrive at a more robust clinical diagnosis of the patients and set an initial foundation of creating a mtDNA variant database in Sri Lanka.

Key words: mitochondrial disease, rare genetic diseases, novel variants, *MT-ND1* gene

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