Mitochondrial disorders: insights into diagnosis and management in the new era of genomic medicine

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Introduction

Mitochondrial diseases are a group of rare inherited disorders characterized by extreme phenotypic heterogeneity that can be transmitted by any mode of inheritance, with hitherto no effective therapy options. The recent evaluations of Next Generation Sequencing for mitochondrial disorders have shown that this methodology is more likely to provide a diagnosis, being quicker and cheaper.
Our group, pioneer in the study of these disorders in our country, has been studying several patients with suspicious diagnosis of mitochondrial disorders. The biochemical and molecular approach used, allowed the characterization of many of these patients, however, some of them still remain without molecular diagnosis.

Objectives

The overall aim of our research project* was to develop a Next Generation Sequencing strategy to identify nuclear disease causing-mutations in patients suspicious of mitochondrial disorders but without molecular etiology.

Methods

Next Generation Sequencing was performed in a MiSeq Illumina instrument using a custom mitochondrial gene panel with around 200 genes involved in mitochondria metabolism. Libraries were prepared using SureSelect QXT target enrichment system from Agilent.

Results

Until now, we analyzed 20 patients, identifying disease related mutations in six of them. These mutations were confirmed by Sanger Sequencing in the index cases and in their relatives.
Our project is ongoing and the patients undiagnosed after this first approach will be further selected for Whole Exome Sequencing.

Discussion and Conclusion

This study is contributing to i) identify the pathogenic mutations in the studied patients (6/20 – 30%), ii) expand the mutational spectrum in the etiology of these disorders, and iii) propose an accurate genetic counseling.
Custom design panels have been widely used for molecular heterogeneous disorders however, the development of this panel will be innovative in our country strengthening our center as a national reference for the study and research of mitochondrial disorders.

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