CENTOGENE
THE RARE DISEASE COMPANY

CASE STUDY

Identifying a Clinically Relevant Mitochondrial Variant With CentoXome®

At CENTOGENE, we are committed to revolutionizing rare disease patient care – continuously striving to provide you and your patients with the best possible medical solutions every step of the way.

The first step: Choosing the right genetic test to efficiently establish or confirm a diagnosis and guide appropriate medical care and prognosis. Keep reading to learn more about how CentoXome, our enhanced Whole Exome Sequencing (WES) solution, is helping physicians around the world to diagnose patients promptly and with the highest levels of certainty.

Clinical Overview

20-year-old female patient

Abnormal electroencephalography (EEG), increased serum lactate, recurrent headaches, abnormal social behavior, seizures (i.e., nocturnal seizures, generalized tonic-clonic seizures), difficulties during breastfeeding, intellectual disability, stroke-like episodes

Parents are nonconsanguineous

Clinical suspicion of mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes (MELAS)

Previous Genetic Testing Performed

- Negative mitochondrial genome deletion/duplication analysis by multiplex ligation-dependent probe amplification (MLPA) at an external lab
- No deletions/duplications related to her clinical diagnosis were found

Testing Strategy

The physician opted for CentoXome to rule out MELAS syndrome and to identify the cause of the disease to enable guidance for the best available treatment options.

Diagnosis of MELAS

CentoXome identified a pathogenic variant (NC_012920.1:m.13513G>A) in the mitochondrial gene *MT-ND5* in a heteroplasmic state (40%), which has been described as causing MELAs. Additionally, no other variant was identified, including copy number variants (CNVs), as clinically relevant for the patient clinical presentation. CENTOGENE's CentoXome then confirmed the genetic diagnosis of MELAS syndrome. Maternal targeted testing was recommended to stablish the origin of the variant (inherited or de novo).

Testing Impact

CentoXome established a definitive diagnosis as a result of its superior design, our extensive clinical experience, and wealth of genetic data in rare diseases. With highly uniform coverage across the entire exome and mitochondrial genome, nearly 100% coverage of approx. 8,000 clinically associated genes and more than 99% of all known disease-causing variants throughout the genome. CentoXome delivers an increased diagnostic yield by up to 20% compared to standard WES, and like in this case, is able to detect variants in mitochondrial encoded genes that often go unseen. The family received genetic counselling and guidance for available treatment options .

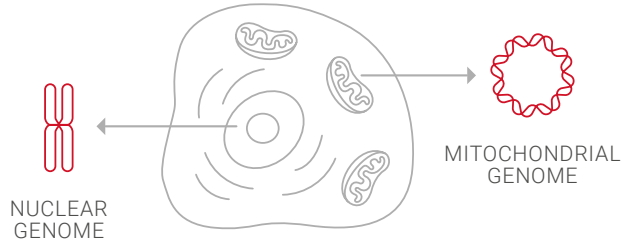

Figure 1: Visual representation of a human cell with nuclear and mitochondrial DNA in the nucleus and mitochondria, respectively. The combined analysis enables the diagnosis of mitochondrial diseases in patients caused by variants in either DNAs or other non-mitochondrial diseases that resemble mitochondrial disorders.

CentoXome can provide superior assessment of genetic variants, both in the nuclear and mitochondrial encoded genes, in a single test and accelerate medical solutions for your patients