TEST ID: MITOP

MITOCHONDRIAL FULL GENOME ANALYSIS BY NEXT GENERATION SEQUENCING (NGS)

USEFUL FOR
- Diagnosis of the subset of mitochondrial diseases that results from mutations in the mitochondrial genome
- A second-tier test for patients in whom previous targeted gene mutation analyses for specific mitochondrial disease-related genes was negative
- Identifying mutations within genes of the mitochondrial genome that are known to be associated with mitochondrial disease, allowing for predictive testing of at-risk family members

GENETICS TEST INFORMATION

This test includes amplification of the entire mitochondrial genome by long-range polymerase chain reaction (LRPCR) followed by sequencing on both the Illumina and Ion Torrent next-generation sequencing (NGS) platforms to evaluate for mutations within the mitochondrial genome.

CLINICAL INFORMATION

The mitochondrion occupies a unique position in eukaryotic biology. First, it is the site of energy metabolism, without which aerobic metabolism and life as we know it would not be possible. Second, it is the sole subcellular organelle that is composed of proteins derived from 2 genomes, mitochondrial and nuclear. A group of hereditary disorders due to mutations in either the mitochondrial genome or nuclear mitochondrial genes have been well characterized.

The diagnosis of mitochondrial disease can be particularly challenging as the presentation can occur at any age, involving virtually any organ system, and with widely varying severities. This test utilizes massively parallel sequencing, also termed next-generation sequencing (NGS) to determine the exact sequence of the entire 16,568 base-pair mitochondrial genome. The utility of this test is to assist in the diagnosis of the subset of mitochondrial diseases that result from mutations in the mitochondrial genome (mtDNA). This includes certain types of myopathies and neuro-opthalomologic diseases, such as mitochondrial encephalomyopathy, lactic acidosis, stroke-like episodes (MELAS), myoclonic epilepsy with ragged red fibers (MERRF), mitochondrial myopathy (MM), neurogenic muscle weakness, ataxia, retinitis pigmentosa (NARP), Leigh syndrome, Leber hereditary optic neuropathy (LHON), and chronic progressive external ophthalmoplegia (CPEO). In addition to the detection of single base changes with these disorders, large deletions, such as those associated with Kearns-Sayre or Pearson syndromes, are also detected. Mutations in mitochondrial proteins that are encoded by genes in the nucleus, such as the enzymes of fatty acid oxidation, are not detected using this test.

REFERENCE VALUES

An interpretive report will be provided.

ANALYTIC TIME

8 weeks

CONTENT AND VALUES SUBJECT TO CHANGE. SEE THE MAYO MEDICAL LABORATORIES TEST CATALOG FOR CURRENT INFORMATION.
In contrast to mutations in nuclear genes, which are present in either 0, 1, or 2 copies, mitochondrial mutations can be present in any fraction of the total organelles, a phenomenon known as heteroplasmy. Typically, the severity of disease presentation is a function of the degree of heteroplasmy. Individuals with a higher fraction of mutant mitochondria present with more severe disease than those with lower percentages of mutant alleles. The sensitivity for the detection of mutant alleles in a background of wild-type (or normal) mitochondrial sequences by NGS is approximately 10%.

INTERPRETATION

All detected alterations are evaluated according to American College of Medical Genetics and Genomics recommendations. Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance. The degree of heteroplasmy of each single nucleotide or INDEL variant, defined as the ratio (percentage) of variant sequence reads to the total number of reads, will also be reported. Large deletions will be reported as either homoplasmic or heteroplasmic, but the degree of heteroplasmy will not be estimated, due to possible preferential amplification of the smaller deletion product by long-range PCR.

CLINICAL REFERENCE

