Mitochondrial Diseases - Nuclear Genes Only: Sequencing Panel

Test Code: MM300
Turnaround time: 6 weeks
CPT Codes: 81406 x1, 81404 x1, 81405 x1

Condition Description

Mitochondrial diseases are a group of disorders caused by mutations in either mitochondrial DNA (mtDNA) or nuclear genes (nDNA). Production of energy in mitochondria, by means of oxidative phosphorylation, strictly depends upon factors which are encoded both by the mtDNA and the nDNA. Respiratory chain complexes are formed, for the most part by subunits of nuclear origin, as are several indispensable complex-assembling proteins. Accurate replication and efficient maintenance of mtDNA are also essential for the respiratory chain to function properly.

Many metabolic processes, distinct from ATP production, are fulfilled in mitochondria: for instance, important steps of metal cation metabolism take place in the mitochondrial matrix. Furthermore, mitochondria actively fuse and divide, and move interacting with the cytoskeleton. All these functions require the expression of nDNA. Mitochondrial disorders caused by nDNA defects have been the object of increasing attention in the past few years, establishing themselves as an important and relatively prevalent group of pathologies, and challenging the relevance of disease caused by inherited mutations of mtDNA itself.

In addition to mtDNA genome sequencing (see related tests), EGL Genetics offers this complementary panel that sequences 44 nuclear mitochondria genes through next generation sequencing technology. This technology is an excellent tool for obtaining gene sequences rapidly and accurately since it allows deep coverage of the genome through multiple independent sequence reads.

References:

- OMIM.
- GeneReviews.

Genes

ATP5A1, BCS1L, COX10, COX15, COX4I1, COX4I2, COX6B1, FASTKD2, FBXL4, FOXRED1, LRPPRC, NDUFA1, NDUFA10, NDUFA11, NDUFA13, NDUFA2, NDUFA6, NDUFAF1, NDUFAF3, NDUFAF4, NDUFAF5, NDUFS1, NDUFS2, NDUFS3, NDUFS4, NDUFS5, NDUFS6, NDUFS7, NDUFS8, NDUFV1, NDUFV3, NUBP1, POLG, SCO1, SCO2, SDHAF1, SDHAF2, SDHAF3, SDHB, SDHC, SDHD, SURF1, TACO1, TMEM70, TTC19, UQCRB, UQCRQ

Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of mitochondrial diseases.

Methodology

**Next Generation Sequencing:** In-solution hybridization of all coding exons is performed on the patient's genomic DNA. Although some deep intronic regions may also be analyzed, this assay is not meant to interrogate most promoter regions, deep intronic regions, or other regulatory elements, and does not detect single or multi-exon deletions or duplications. Direct sequencing of the captured regions is performed using next generation sequencing. The patient's gene sequences are then compared to a standard reference sequence. Potentially causative variants and areas of low coverage are Sanger-sequenced. Sequence variations are classified as pathogenic, likely pathogenic, benign, likely benign, or variants of unknown significance. Variants of unknown significance may require further studies of the patient and/or family members.

Detection

**Next Generation Sequencing:** Clinical Sensitivity: Unknown. Mutations in the promoter region, some mutations in the introns and other regulatory element mutations cannot be detected by this analysis. Large deletions/duplications will not be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's clinical/biochemical phenotype.

Analytical Sensitivity: ~99%.

Specimen Requirements

*Submit only 1 of the following specimen types*

**Type:** Saliva

**Specimen Requirements:**
Oragene™ Saliva Collection Kit
Orangene™ Saliva Collection Kit used according to manufacturer instructions. Please contact EGL for a Saliva Collection Kit for patients that cannot provide a blood sample.

**Specimen Collection and Shipping:**
Please do not refrigerate or freeze saliva sample. Please store and ship at room temperature.

**Type: DNA, Isolated**

**Specimen Requirements:**
- Microtainer
- 8µg
- Isolation using the Perkin Elmer™Chemagen™ Chemagen™ Automated Extraction method or Qiagen™ Puregene kit for DNA extraction is recommended.

**Specimen Collection and Shipping:**
Refrigerate until time of shipment in 100 ng/µL in TE buffer. Ship sample at room temperature with overnight delivery.

**Type: Whole Blood (EDTA)**

**Specimen Requirements:**
- EDTA (Purple Top)
- Infants and Young Children (2 years of age to 10 years old): 3-5 ml
- Older Children & Adults: 5-10 ml
- Autopsy: 2-3 ml unclotted cord or cardiac blood

**Specimen Collection and Shipping:**
Ship sample at room temperature for receipt at EGL within 24 hours of collection. Do not refrigerate or freeze.

**Related Tests**
- Mitochondrial Genome: Sequencing
- Mitochondrial Diseases - Nuclear Genes Only: Deletion/Duplication Panel