Mitochondrial Encephalomyopathy: Lactic Acidosis (Stroke-like Episodes/MELAS)

**Test Code:** QA  
**Turnaround time:** 3 weeks  
**CPT Codes:** 81401 x1

### Condition Description

MELAS is characterized by mitochondrial encephalomyopathy, lactic acidosis, stroke-like episodes, often presenting in childhood. Other common symptoms include seizures, muscle weakness, recurrent headaches and vomiting, and exercise intolerance. Sensorineural hearing loss may also occur. Symptoms are highly variable, in part due to the amount of heteroplasmy (i.e., both normal and mutant mitochondrial DNAs are present in the same cell) and tissue distribution of abnormal mitochondria (replicative segregation). Symptoms may worsen during times of stress or illness.

Mutations in the MTTL1 mitochondrial gene (tRNA-Leu) have been identified in patients with MELAS. Mutations in MTTL1 can result in impaired mitochondrial respiratory chain complex I and cytochrome C oxidase activity. Reduction in mitochondrial respiratory chain function reduces that amount of ATP produced by the mitochondria.

The most common mutation in MTTL1, present in over 80% of patients with typical clinical findings of MELAS, is a 3243A>G transition in MTTL1. The MTTL1 mutations 3,271 T>C, 3,252 A>G, 3,291 T>C, and 3,260 A>G account for an additional 15-20% of all MELAS mutations. Other rare mutations in the MTTL1 gene have also been observed. MTTL1 mutations outside the MTTL1 gene have been described in rare cases. Mutations associated with MELAS may be heteroplasmic with the degree of heteroplasmy varying in different tissues. Based on clinical presentation, either a blood or a tissue sample (muscle biopsy) may be used.

### Indications

- Patients with a confirmed or suspected diagnosis of MELAS.  
- Family members of an affected patient who are at risk for MELAS.

### Methodology

The MTTL1 mitochondrial gene (tRNA-Leu) is PCR amplified and sequenced in both the forward and reverse directions. The 3243A>G mutation is analyzed by a sensitive allele-specific extension assay to reliably detect heteroplasmic mutations. Patient gene sequences are compared to a normal reference sequence. Sequence variations are then classified as previously described mutations, novel mutations, or variations of unknown significance. This assay may detect variants of MTTL1 that may require further studies.

### Detection

This assay will detect over 90% of mitochondrial mutations associated with MELAS. The 3243A>G mutation can be detected at approximately 10% heteroplasmy. All other mutations can be detected at approximately 15-20% heteroplasmy. Mutations outside the MTTL1 gene will not be detected.

### Reference Range

Qualitative assay.

### Specimen Requirements

- **Submit only 1 of the following specimen types**

#### 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 72 hours of collection. Do not freeze.

#### 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: 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.

### Related Tests
- MERRF (OH) Testing may be indicated for patients who also show progressive external ophthalmoplegia and ragged red fibers on muscle biopsy
- KSS/CPEO (QB) Testing may be indicated for patients who also show progressive external ophthalmoplegia
- Myotonic Dystrophy (MD) may be indicated for patients who show muscle weakness