Myoclonic Epilepsy and Ragged-Red Fiber Disease (MERRF): Targeted Mutation Analysis

Test Code: QH
Turnaround time: 2 weeks
CPT Codes: 81401 x1

**Condition Description**

Myoclonic Epilepsy & Ragged-Red Fiber Disease (MERRF) usually presents during childhood and is characterized by myoclonus, epilepsy, ataxia, and the appearance of ragged-red fibers on muscle biopsy. Other common symptoms include hearing loss, peripheral neuropathy, dementia, short stature, optic atrophy, cardiomyopathy, and exercise intolerance. Symptoms may worsen during times of stress or illness. Two mutations the mitochondrial tRNA Lys gene account for about 90% of mutations in patients with MERRF. The most common MERRF mutation, present in over 80% of patients with typical findings, is a heteroplasmic 8344A>G transition. A second mutation, 8356T>C, is present in less than 10% of patients.

Heteroplasmy (the presence of both normal and rearranged mitochondrial DNA molecules) and tissue distribution of abnormal mitochondria (replicative segregation) can result in variability of clinical symptoms. Mitochondrial tRNA Lys gene mutations result in multiple mitochondrial respiratory chain deficiencies. Enzyme deficiencies, which are most pronounced in complex I and complex IV, are secondary to defects in mitochondrial protein synthesis caused by mutations in tRNA Lys. MERRF caused by mtDNA mutations is maternally inherited. It is estimated that approximately 80% of patients have a family history of the disorder.

References:

- Gene Reviews Clinical Summary

**Genes**

tRNA Lys

**Indications**

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

**Methodology**

Presence or absence of two mutations (8344A>G / 8356T>C) are detected by Sanger sequencing.

**Detection**

Approximately 85-90% of patients with MERRF have mitochondrial mutations included in this panel. Over 95% of the 8344A>G and 8356T>C mutations, if present, will be detected. This assay will detect any mutation on this panel present at 15-20% heteroplasmy or greater.

**Reference Range**

Qualitative assay.

**Specimen Requirements**

Submit only 1 of the following specimen types

**Type: Whole Blood**

Specimen Requirements:

In EDTA (purple top) tube:
- Infants (2 years): 3-5 ml
- Older Children & Adults: 5-10 ml

Specimen Collection and Shipping: Refrigerate until time of shipment. Ship sample within 5 days of collection at room temperature with overnight delivery.

**Type: Muscle Biopsy**

Specimen Requirements:

1-2 mm in length or > 100 mg is acceptable.

Flash freeze sample upon collection using liquid nitrogen. If storage is required, store sample at -80°C or colder.

Specimen Collection and Shipping: Ship frozen sample on dry ice with overnight delivery.

**Related Tests**

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- MELAS (QA) may be indicated for patients who also have strokes
- CPEO/KSS (QB) may be indicated for patients who also have progressive external ophthalmoplegia and retinopathy