Carnitine Deficiency, Primary (Carnitine Uptake Defect): **SLC22A5** Gene Deletion/Duplication

**Condition Description**

Carnitine deficiency is an autosomal recessive disorder of fatty acid oxidation [1]. Deficiency of the sodium ion-dependent carnitine transporter (OCTN2), increases urinary carnitine losses and produces carnitine deficiency in affected tissues. Since carnitine is required for the entry of long-chain fatty acids into mitochondria, carnitine deficiency impairs mitochondrial fatty acid beta-oxidation and subsequent energy production, especially during fasting or illness.

Carnitine deficiency can be identified in infants by expanded newborn screening using tandem mass spectrometry which may detect low levels of free carnitine (C0) [2-3]. If untreated, affected patients typically present in childhood with hypoketotic hypoglycemia, hepatic encephalopathy, hypotonia, cardiomyopathy, or sudden death.

Treatment with oral carnitine at pharmacologic levels is quite effective in treating cardiomyopathy and muscle weakness in these children. In some cases, neonatal screen results of low C0 are due to primary carnitine deficiency in their affected mothers [4]. Primary or systemic carnitine deficiency is distinct from secondary carnitine deficiency, which may be a symptom of other mitochondrial beta-oxidation disorders.

Carnitine deficiency is caused by mutations in the **SLC22A5** (5q31) gene encoding the sodium ion-dependent carnitine transporter (OCTN2) [5-6]. There is some evidence for genotype and phenotype variation [8] but well established associations are limited [9-10]. Diagnosis is based on the identification of very low C0 levels in plasma and is confirmed by the measurement of diminished OCTN2 activity in skin fibroblasts or mutational analysis of the **SLC22A5** gene [7]. Gene sequence analysis is available to test for mutations in the **SLC22A5** gene.

**References:**

**Genes**

**SLC22A5**

**Indications**

This test is indicated for:
- Confirmation of a clinical/biochemical of carnitine deficiency.
- Carrier testing in adults with a family history of carnitine deficiency.

**Methodology**

DNA isolated from peripheral blood is hybridized to a CGH array to detect deletions and duplications. The targeted CGH array has overlapping probes which cover the entire genomic region.

Please note that a "backbone" of probes across the entire genome are included on the array for analytical and quality control purposes. Rarely, off-target copy number variants causative of disease may be identified that may or may not be related to the patient's phenotype. Only known pathogenic off-target copy number variants will be reported. Off-target copy number variants of unknown clinical significance will not be reported.

**Detection**

Detection is limited to duplications and deletions. The CGH array will not detect point or intronic mutations.

Results of molecular analysis must be interpreted in the context of the patient's clinical and/or biochemical phenotype.

**Specimen Requirements**
Submit only 1 of the following specimen types

* Preferred specimen type: Whole Blood

**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: Saliva**

Specimen Requirements:

Oragene™ Saliva Collection kit (available through EGL) used according to manufacturer instructions.

Specimen Collection and Shipping: Store sample at room temperature. Ship sample within 5 days of collection at room temperature with overnight delivery.

**Special Instructions**

Please submit copies of diagnostic biochemical test results along with the sample. Sequence analysis is required before deletion/duplication analysis by targeted CGH array. If sequencing is performed outside of EGL Genetics, please submit a copy of the sequencing report with the test requisition.

**Related Tests**

- Organic Acids - Urine (OA), and Acylcarnitine Profile - Plasma(AR) are used in the diagnosis of a patient with CUD.
- **Known Mutation Analysis (KM)** is available to family members if mutations are identified by sequencing.
- Prenatal Custom Diagnostics is available for known familial mutations only. Please call the laboratory genetic counselor before collecting a fetal sample.