Carnitine-Acylcarnitine Translocase Deficiency: SLC25A20 Gene Deletion/Duplication

**Condition Description**

Mitochondrial oxidation of fatty acids provides the chief source of energy during prolonged fasting as well as for skeletal muscle during exercise and for cardiac muscle. Carnitine-acylcarnitine translocase is 1 of 10 closely related mitochondrial-membrane carrier proteins that shuttle substrates between cytosol and the intramitochondrial matrix space. Other genetic defects in this pathway can cause LCAD deficiency, MCAD deficiency, SCAD deficiency, CPT I deficiency, and CPT II deficiency. Patients with these defects present with coma after a period of starvation and have low serum ketone concentrations (hypoketotic hypoglycemia). They may also have hyperammonemia, hepatomegaly, cardiomyopathy and muscle weakness.

Carnitine-acylcarnitine translocase deficiency is a rare autosomal recessive disorder of fatty acid oxidation. CACT is the second component of the carnitine shuttle for the import of long-chain fatty acids from the cytosol into the mitochondrion where they undergo oxidation. It is an inner mitochondrial membrane protein which mediates the transport of acylcarnitine esters into the mitochondrial matrix in exchange for free carnitine.

CACT deficiency is caused by mutations in the SLC25A20 gene (3p21.31). CACT deficiency is, together with infantile carnitine palmitoyltransferase II (CPT2) deficiency, the most severe of the mitochondrial fatty acid oxidation defects. The pathogenesis of the disorder is a combination of the deficient production of energy from mitochondrial fatty acid oxidation and the toxicity of accumulating long-chain acylcarnitines. It usually presents in the early newborn period, with a high mortality at the initial presentation or during the first year of life. The typical features include:

- cardiomyopathy
- arrhythmias
- hepatic dysfunction
- skeletal muscle damage
- hyperammonemia
- hypoketotic hypoglycemia with dicarboxylic aciduria
- elevation of long-chain acylcarnitines
- deficiency of free carnitine

A minority of patients have a later onset with a milder clinical phenotype. In a significant proportion of cases, the presentation is as sudden, unexpected death, presumably due to an arrhythmia.

Please click here for the OMIM summary on this gene and condition.

Reference:

**Genes**

SLC25A20

**Indications**

This test is indicated for:

- Confirmation of a clinical/biochemical diagnosis of CACT deficiency.
- Carrier testing in adults with a family history of CACT 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. Contact the laboratory if further information is needed.

**Related Tests**

- Known Mutation Analysis (KMA) is available to family members if mutations are identified by sequencing.
- Prenatal Custom Diagnostics is available to couples who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.