Carnitine Palmitoyltransferase 1A Deficiency: \textit{CPT1A} Gene Deletion/Duplication

\textbf{Test Code:} PZ  
\textbf{Turnaround time:} 2 weeks  
\textbf{CPT Codes:} 81228 x1

\textbf{Condition Description}

Carnitine palmitoyltransferase 1A (CPT1A) deficiency is an autosomal recessive disorder of long-chain fatty acid oxidation. Onset of symptoms is typically rapid, and occurs during febrile or gastrointestinal illness when energy demands are increased. Between episodes, individuals may appear developmentally and cognitively normal, unless previous metabolic decompensation has resulted in neurological damage. There are three types of CPT1A: hepatic encephalopathy, adult-onset myopathy, and acute fatty liver of pregnancy. In hepatic encephalopathy, children present with hypoketotic hypoglycemia and sudden onset of liver failure. Adult-onset myopathy has been observed in one individual of Inuit ancestry, whose presenting feature was a history of exercise-induced sudden-onset muscle cramping. Acute fatty liver of pregnancy occurs when the fetus has CPT1A deficiency.

Typical laboratory findings are hypoglycemia, absent or low levels of ketones, elevated liver transaminases, elevated serum ammonia concentration, and elevated total serum carnitine. In most affected individuals, CPT I enzyme activity in cultured skin fibroblasts accounts for 1%-5% of control activity. Screening for CPT1A deficiency by detecting an elevated ratio of free-to-total carnitine in serum or plasma on a blood spot is available in some state newborn screening programs.

\textit{CPT1A} (11q13) is the only gene associated with CPT1A deficiency.

For patients with suspected CPT1A, sequence analysis is recommended as the first step in mutation identification. For patients in whom mutations are not identified by full gene sequencing, deletion/duplication analysis is appropriate.

\textbf{References:}

- GeneReviews Clinical Summary

\textbf{Genes}

\textbf{CPT1A}

\textbf{Indications}

This test is indicated for:

- Confirmation of a clinical/biochemical diagnosis of CPT1A deficiency in individuals who have tested negative for sequence analysis
- Carrier testing in adults with a family history of CPT1A deficiency who have tested negative for sequence analysis

\textbf{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.

\textbf{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.

\textbf{Specimen Requirements}

Submit only 1 of the following specimen types

- Preferred specimen type: Whole Blood

**Type:** Whole Blood

Specimen Requirements:

In EDTA (purple top) or ACD (yellow 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
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. Sequence analysis is required before deletion/duplication analysis by targeted CGH array. If sequencing is performed outside of Emory Genetics Laboratory, please submit a copy of the sequencing report with the test requisition.

Related Tests

- Sequencing analysis of the CPT1A gene is available and is required before deletion/duplication analysis.
- Known Mutation Analysis (KM) is available to family members if mutations are identified by targeted mutation testing or sequencing analysis.
- 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.