Succinyl-CoA, 3-Oxoacid CoA Transferase (SCOT) Deficiency: \textit{OXCT1} Gene Sequencing

**Condition Description**

Succinyl-CoA-3-oxoacid CoA transferase (SCOT) deficiency causes episodic ketoacidosis without symptoms between episodes. Persistent ketoacidosis and ketonuria are characteristic of the disease, but may be absent in some affected individuals. Almost half of individuals with SCOT deficiency will develop the first ketoacidotic crisis at the age of 2-4 days. Affected individuals are generally physically and developmentally normal.

No diagnostic metabolites are observed in the blood and urine sample from SCOT-deficient individuals, in contrast to most organic acidemias. Ketone bodies, acetocaceteate, and 3-hydroxybutyrate are, however, elevated. SCOT deficiency is caused by mutations in the \textit{OXCT1} gene (5p14). It is inherited in an autosomal recessive manner. SCOT is a mitochondrial homodimer essential for ketone body utilization. Ketone bodies, which are produced in the liver, are an important source of energy for extrahepatic tissues.

**References:**
- OMIM \#245050  SCOT Deficiency.
- OMIM \#601424  \textit{OXCT1}.

**Genes**

\textit{OXCT1}

**Indications**

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

**Methodology**

**Next Generation Sequencing:** In-solution hybridization of all coding exons is performed on the patient's genomic DNA. Although some deep intronic regions may also be analyzed, this assay is not mean to interrogate most promoter regions, deep intronic regions, or other regulatory elements, and does not detect single or multi-exon deletions or duplications. Direct sequencing of the captured regions is performed using next generation sequencing. The patient's gene sequences are then compared to a standard reference sequence. Potentially causative variants and areas of low coverage are Sanger-sequenced. Sequence variations are classified as pathogenic, likely pathogenic, benign, likely benign, or variants of unknown significance. Variants of unknown significance may require further studies of the patient and/or family members.

**Detection**

Clinical Sensitivity: Unknown. Mutations in the promoter region, some mutations in the introns and other regulatory element mutations cannot be detected by this analysis. Large deletions will not be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's biochemical phenotype.

Analytical Sensitivity: ~99%.

**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 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

Submit copies of diagnostic biochemical test results with the sample, if appropriate. Contact the laboratory if further information is needed.

### Related Tests

- Custom diagnostic mutation analysis (KM) is available to family members if mutations are identified by targeted mutation testing or sequencing analysis.
- Prenatal testing is available only for known familial mutations to individuals who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.