Malonyl-CoA Decarboxylase Deficiency: MLYCD Gene Sequencing

**Condition Description**

Malonyl-CoA decarboxylase (MCD) deficiency is an autosomal recessive disorder of fatty acid metabolism characterized by malonic aciduria, developmental delay, seizures, hypoglycemia, and cardiomyopathy. Other features may include acidosis, short stature, hypotonia, and lethargy. MCD deficiency has a variable presentation with different phenotypes observed in siblings, and can have clinical overlap with fatty acid oxidation disorders.

MCD deficiency results in elevated levels of serum malonylcarnitine (C3DC), which is quantified in many newborn screening (NBS) programs. Mutations in the MLYCD gene (16q24) cause MCD deficiency. Both point mutations and deletions have been reported in the MLYCD gene in affected individuals. Wightman et al. reported finding 16 of 18 MLYCD mutations in nine affected individuals (2003); Salomons et al. reported finding 18 of 18 mutations in nine other affected individuals (2007).

**References:**

**Genes**

**MLYCD**

**Indications**

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

**Methodology**

PCR amplification of 5 exons contained in the MLYCD gene is performed on the patient's genomic DNA. Direct sequencing of amplification products is performed in both forward and reverse directions, using automated fluorescence dideoxy sequencing methods. The patient's gene sequences are then compared to a normal reference sequence. Sequence variations are classified as mutations, benign variants unrelated to disease, or variations of unknown clinical significance. Variants of unknown clinical significance may require further studies of the patient and/or family members. This assay does not interrogate the promoter region, deep intronic regions, or other regulatory elements, and does not detect large deletions.

**Detection**

Clinical Sensitivity: Wightman et al. reported finding 16 of 18 MLYCD mutations in nine affected individuals (2003); Salomons et al. reported finding 18 of 18 mutations in nine other affected individuals (2007). 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.

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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.

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**

- 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 to adult females who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.