

## Medium Chain Acyl Co-A Dehydrogenase (MCADD): *ACADM* Gene Sequencing

**Test Code:** MV

**Turnaround time:** 4 weeks

**CPT Codes:** 81479 x1

### Condition Description

Medium chain acyl-CoA dehydrogenase deficiency (MCADD) is an autosomal recessive disorder of fatty acid oxidation, the process by which the body metabolizes fats for energy in the absence of glucose. MCAD deficiency results in the inability to break down medium sized fatty acids (6-12 carbon atoms in length). As a result, these fatty acids accumulate mainly in the liver and to a lesser extent in the heart and kidneys.

MCADD generally presents between two months and two years of life, but can present as early as two days of life and as late as adulthood. Affected children are healthy and usually asymptomatic until symptoms are triggered by prolonged fasting or an illness that causes a decreased caloric intake, like the flu, a cold, or an ear infection. The inability to convert fats to energy can lead to:

- hypoglycemia
- vomiting
- lethargy
- coma
- apnea
- cardiac arrest
- sudden unexplained death

About 20-25% of MCADD patients die from their first symptomatic episode. MCADD is believed to account for up to 2.5% of sudden infant death syndrome (SIDS) cases.

MCADD results from mutations in the acyl-CoA dehydrogenase, medium-chain (*ACADM*) gene located on chromosome 1p31. The MCAD protein functions within the mitochondria at the first step in beta-oxidation of medium chain fatty acids. Sequencing of *ACADM* is recommended for patients with a biochemical diagnosis of MCADD as a complementary method to confirm the presence of mutations in a proband, to identify carriers among the probands relatives, and to provide prenatal diagnosis in families with known mutations. Sequencing is recommended only after mutation analysis for the *K304E* and *Y42H* mutations has been performed. For patients with mutations not identified by full gene sequencing, a separate deletion/duplication assay is available using a targeted CGH array.

Reference:

Andresen et al. (2001) Am J Hum Genet 68: 1408-1418.

### Genes

[ACADM](#)

### Indications

This test is indicated for:

- Patients who are found to have symptoms of MCADD (including elevated urine dicarboxylic acids and/or elevated medium chain acylcarnitines).
- Infants who are hypoglycemic, have unexplained seizures, or have a family history of SIDS (Sudden Infant Death Syndrome).
- Patients with symptoms of MCADD with only one/no mutations identified through the common mutation panel.

### Methodology

The 12 coding exons and immediate flanking regions of *ACADM* are amplified by PCR and sequenced in both forward and reverse directions. The patient's gene sequences are then compared to a normal reference sequence. Sequence variations are classified as previously described mutations, novel mutations, or variations of unknown significance. This analysis may detect novel variants of unclear effect that require further studies.

### Detection

This assay will detect over 97% of the sequence variants in the coding region and splice junctions. Mutations in the promoter region, some mutations in the introns and other regulatory elements, large deletions, and insertion mutations will not be detected by this assay.

Results of molecular analysis should be interpreted in the context of the patient's biochemical phenotype.

### Specimen Requirements

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

**Type: DNA, Isolated**

**Specimen Requirements:**

Microtainer

8µg

Isolation using the Perkin Elmer™ Chemagen™ Chemagen™ Automated Extraction method or Qiagen™ Puregene kit for DNA extraction is

recommended.

**Specimen Collection and Shipping:**

Refrigerate until time of shipment in 100 ng/ $\mu$ L in TE buffer. Ship sample at room temperature with overnight delivery.

**Type: Whole Blood (EDTA)****Specimen Requirements:**

EDTA (Purple Top)

Infants and Young Children ( 2 years of age to 10 years old: 3-5 ml

Older Children & Adults: 5-10 ml

Autopsy: 2-3 ml unclotted cord or cardiac blood

**Specimen Collection and Shipping:**

Ship sample at room temperature for receipt at EGL within 24 hours of collection. Do not refrigerate or freeze.

**Type: Saliva****Specimen Requirements:**

Oragene™ Saliva Collection Kit

Oragene™ Saliva Collection Kit used according to manufacturer instructions. Please contact EGL for a Saliva Collection Kit for patients that cannot provide a blood sample.

**Specimen Collection and Shipping:**

Please do not refrigerate or freeze saliva sample. Please store and ship at room temperature.

**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 EGL Genetics, please submit a copy of the sequencing report with the test requisition.

**Related Tests**

- Acylcarnitine Analysis - Plasma (PA) and Organic Acid Analysis (OA) are used in the diagnosis and evaluation of patients with metabolic conditions, such as MCADD.
- MCADD Common Mutation Analysis (MC) is available for the K304E and Y42H mutations, prior to sequencing.
- [Known Mutation Analysis \(KM\)](#) is available to family members if mutations are identified by sequencing.
- Deletion/Duplication Assay is available separately for individuals where mutations are not identified by sequence analysis. Refer to the test requisition or contact the laboratory for more information.
- Prenatal testing 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.