Medium Chain Acyl-CoA Dehydrogenase (MCADD): ACADM Common Mutation Panel

Test Code: MC  
Turnaround time: 2 weeks  
CPT Codes: 81401 x1

Condition Description

Medium chain acyl-CoA dehydrogenase deficiency, or 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. Specifically, this enzyme deficiency results in the inability to break down fatty acids that are considered medium in size (6-12 carbon atoms in length). As a result, these fatty acids accumulate mainly in the liver, but also 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, or 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. This test offers mutation analysis for the common ADADM gene mutations, K304E and Y42H, which are most common in individuals of Caucasian, specifically Northern European, background.

References:
- GeneReviews Clinical Summary

Genes

ACADM

Indications

This test is indicated for:
- Patients who are found to have 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).
- Siblings of an individual with diagnosed with MCADD who present with clinical symptoms of MCADD or to determine parental carrier status.

Methodology

Presence or absence of the K304E and Y42H mutations are detected by Sanger sequencing.

Detection

All K304E or Y42H mutant alleles will be detected by this assay. At least one copy of the K304E mutation is present in approximately 97% of individuals with MCADD. Two copies (homozygosity) of K304E mutation is present in approximately 63%. Y42H is the next most common mutation found in 12% of patients with MCADD.

Reference Range

Qualitative assay.

Specimen Requirements

Submit only 1 of the following specimen types

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 72 hours of collection. Do not freeze.

Type: DNA, Isolated

Specimen Requirements:
Microtainer
3µg

Disclaimer: This information is confidential and subject to change without notice. It may not be reproduced in whole or part unless authorized in writing by an authorized EGL representative.
Isolation using the Perkin Elmer™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/µL in TE buffer. Ship sample at room temperature with overnight delivery.

**Related Tests**
- Plasma Acylcarnitine (PA) and Organic Acid Analysis (OA) are used in the diagnosis and evaluation of patients with metabolic conditions, such as MCADD.
- MCADD Sequencing (MV) is available for patients with unidentified mutations.
- Prenatal testing is available to couples who are confirmed carriers of MCADD mutations. Please contact the laboratory genetic counselor to arrange prior to collecting a prenatal specimen.