

# MEDIUM CHAIN ACYL-CoA DEHYDROGENASE DEFICIENCY (MCADD)

Comprehensive Test - **Test 1**

- Updated 08-10-09 –

## DESCRIPTION

Mendelian Inheritance in Man number: [\\*607008](#)

Click here for [Gene Reviews](#) Clinical Summary.

MCADD is the most common enzyme deficiency in mitochondrial fatty acid  $\beta$ -oxidation. In a typical clinical scenario, a previously healthy child presents with hypoketotic hypoglycemia, vomiting, and lethargy triggered by a common illness such as fasting or infection. Patients with MCADD also may present encephalopathy, hepatomegaly and acute liver disease, skeletal myopathy, and cardiomyopathy. Apparent life threatening events have also been linked to MCADD. Patients are normal at birth and typically present between three and 24 months of age; later presentation, even into adulthood, is possible. About 18-25% patients die during their first episode of illness. The prognosis is excellent once the diagnosis is established and frequent feedings are instituted to avoid any prolonged period of fasting.

### Genetics of *ACADM*

*ACADM* is the only gene known to be associated with MCADD. It consists of 12 exons that span more than 44 kb and encodes a protein of 421 amino acids. The overall frequency of the disease has been estimated to range between 1:4,900 to 1:17,000, depending on the ethnic composition of the population. One mutation located in exon 11, c.985A>G, p.K329E, is present in approximately 80-90% of alleles in patients with MCADD based on newborn screening results in diverse population. The carrier frequency for the p.K329E mutation of the *ACADM* gene is between 1:40 and 1:100.

## INDICATIONS FOR DIRECT TESTING

- Confirmation of diagnosis for individuals with an abnormal acylcarnitine profile, hypoglycemic episodes, lethargy, seizures or a family history of MCADD

## TESTING METHODOLOGY

For *ACADM* testing, we distinguish 2 types of test requests: targeted mutation analysis of the c.985A>G, p.K329E mutation (**Tier1** testing) and comprehensive sequence analysis of the *ACADM* gene (**Tier 2** testing). Tier 1 is the priority test for the MCADD patients, since the common mutation p.K329E in exon 11 of *ACADM* gene accounts for 80-90% of the mutant alleles. If the patient is heterozygous for the p.K329E mutation or does not carry this most frequent mutation, the comprehensive *ACADM* mutation analysis (Tier 2 testing) is performed.

**Parental testing is performed free of charge, if parental samples are submitted the same week as the sample of the proband.** Parental testing will be performed at charge if parental samples are submitted at a later date.

## **SPECIMEN REQUIREMENTS**

We require 5 milliliters of whole blood. Blood samples must be collected in EDTA (purple topped) tubes.

## **TRANSPORT**

If the specimen is from clinics within UAB or Kirklin Clinic, please call 934-5562 for pickup. If specimens are being sent from some other location, please ship via UPS or Federal Express.

1. Specimens must be packaged to prevent breakage and absorbent material must be included in the package to absorb liquids in the event that breakage occurs. Also, the package must be shipped in double watertight containers (e.g. a specimen pouch + the shipping companies Diagnostic Envelope). **You can use our collection kits, which we will send to physicians directly upon request.**

2. Please contact us (Email – [mgl@genetics.uab.edu](mailto:mgl@genetics.uab.edu), Phone – 205-934-5562) prior to sample shipment and provide us with the **date of shipment** and the **tracking number** of the package.

## **TURN AROUND TIME**

2 weeks

## **CPT CODES AND PRICES**

**Please note that prices listed correspond to institutional rates; please contact the lab for insurance rates.**

**Targeted Analysis of c.985A>G, p.K329E and other possible mutations in exon 11 (Test 1-Tier 1):**

\$190, -USD ([currency converter](#))

83891 (x1), 83894 (x3), 83898 (x3), 83904 (x2), 83912 (x1)

**Complete Sequence of the *ACADM* gene if Tier 1 is negative (Test 1-Tier 2):**

\$600, -USD ([currency converter](#))

83891 (x1), 83894 (x10), 83898 (x10), 83904 (x20), 83912 (x1)

## **REQUIRED FORMS**

[General Requisition](#)

**Note:** Requests for Molecular Genetic testing for MCADD will **not** be accepted for the following reasons:

- No label (patients full name and date of collection) on the specimens
- No referring physician's or genetic counselor's names and addresses
- No billing information
- No informed consent

**For more information, test requisition forms, or sample collection and mailing kits, please call: 205-934-5562.**

## REFERENCES

Andresen BS, Dobrowolski SF, O'Reilly L, Muenzer J, McCandless SE, Frazier DM, Udvari S, Bross P, Knudsen I, Banas R, Chace DH, Engel P, Naylor EW, Gregersen N (2001) Medium-chain acyl-CoA dehydrogenase (MCAD) mutations identified by MS/MS-based prospective screening of newborns differ from those observed in patients with clinical symptoms: identification and characterization of a new, prevalent mutation that results in mild MCAD deficiency. *Am J Hum Genet* 68(6): p. 1408-18. ([pubmed](#))

Gregersen N, Bross P, Andresen BS (2004) Genetic defects in fatty acid beta-oxidation and acyl-CoA dehydrogenases. *Molecular pathogenesis and genotype-phenotype relationships. Eur J Biochem.* 271(3):470-82 ([pubmed](#))

Kozak L, Hrabincova E, Rudolfova J, Vrabelova S, Freiburger T (1999) Screening of the most common medium-chain acyl CoA dehydrogenase (MCAD) deficiency mutation (K329E) in the Czech newborn population. *Southeast Asian J Trop Med Public Health*, 30 Suppl 2: p. 49-50. ([pubmed](#))

Matsubara Y, Narisawa K, Miyabayashi S, Tada K, Coates PM, Bachmann C, Elsas LJ 2<sup>nd</sup>, Pollitt RJ, Rhead WJ, Roe CR (1990) Identification of a common mutation in patients with medium-chain acyl-CoA dehydrogenase deficiency. *Biochem Biophys Res Commun*, 171(1): p. 498-505. ([pubmed](#))