Medium-chain acyl-CoA dehydrogenase (MCAD) deficiency

Disorder:

MCAD deficiency is the most common disorder of fatty acid oxidation affecting 1 in 13,000 newborns and is inherited as an autosomal recessive disorder. This enzyme deficiency results in the inability to catabolize medium-chain (6-12 carbon molecules) fatty acids for energy utilization. MCAD deficiency often presents in the first two years of life after viral illness or fasting. This inability to break down medium-chain lipids as an energy source during times of fasting and metabolic stress can result in hypoglycemia associated with vomiting, lethargy, apnea, coma, encephalopathy and sudden death.

Indications:

- Unexplained low blood sugars and metabolic acidosis in an infant
- Abnormal newborn screen suggesting MCAD deficiency
- Abnormal acylcarnitine profile consistent with MCAD deficiency
- Abnormal organic acid profile consistent with MCAD deficiency
- Presymptomatic testing of at-risk siblings
- Prenatal diagnosis of an at-risk fetus, after confirmation of biallelic mutations in the parents (by prior arrangement only)
- Carrier testing in relative of a patient with MCAD deficiency

Specimen:

At least 3 mLs whole blood in purple/lavender top (EDTA) tube. Label tube with patient's name, birth date, and date of collection. Phlebotomist must initial tube to verify patient's identity.

Test Offerings:

- *ACADM* K329E genotyping only
- *ACADM* full gene sequencing

Test Methodology and Sensitivity:

ACADM K329E SNP genotyping

- This test detects only the K329E allele which accounts for 60-90% of disease causing mutations in *ACADM*. Heterozygous and normal test results may be reflexed to full gene sequencing. An additional charge will apply.

ACADM full gene sequencing PCR-based sequencing of all 12 exons and exon/intron boundaries of the _ACADM_ gene

- PCR-based sequencing detects >95% of patients with MCAD deficiency. The sensitivity of DNA sequencing is over 99% for the detection of nucleotide base changes, small deletions and insertions in the regions analyzed. Multiple exon deletions and insertions may not be identified by this methodology. *ACADM* is the only gene associated with MCAD deficiency.

MetaboSeq fatty acid oxidation defects (FAOD) gene sequencing panel also detects mutations in *ACADM* and 18 other genes involved with FAOD. Please see our website for details.

Turn-Around Time:

- *ACADM* K329E genotyping: 4 days
- *ACADM* full gene sequencing: 28 days

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changing the outcome together

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CPT Codes:

- *ACADM* Genotyping for K329E allele: **81400**
- *ACADM* full gene sequencing: **81479**
- Family specific mutation analysis: **81403**

Results:

Each test report includes a detailed interpretation of the genetic findings, the clinical significance of the result, and specific recommendations for clinical management and additional testing, if warranted. Results will be reported to the referring physician or health care provider as specified on the test requisition form.

References:

Kelly, D. P., J. J. Kim, et al. (1987). Nucleotide sequence of medium-chain acyl-CoA dehydrogenase mRNA and its expression in enzyme-deficient human tissue. Proc Natl Acad Sci U S A 84(12): 4068-4072.

Maier, E. M., B. Liebl, et al. (2005). Population spectrum of ACADM genotypes correlated to biochemical phenotypes in newborn screening for medium-chain acyl-CoA dehydrogenase deficiency. Hum Mutat 25(5): 443-452.

Matern, D. and P. Rinaldo (2000; updated 2012). Medium-Chain Acyl-Coenzyme A Dehydrogenase Deficiency. GeneReviews. R. A. Pagon, T. D. Bird, C. R. Dolan, K. Stephens and M. P. Adam. Seattle (WA).

Smith, E. H., C. Thomas, et al. (2010). Allelic diversity in MCAD deficiency: the biochemical classification of 54 variants identified during 5 years of ACADM sequencing. Mol Genet Metab 100(3): 241-250.

Zhang, Z. F., D. P. Kelly, et al. (1992). Structural organization and regulatory regions of the human medium-chain acyl-CoA dehydrogenase gene. Biochemistry 31(1): 81-89.

Merritt, J. L., 2nd, & Chang, I. J. (2000). Medium-Chain Acyl-Coenzyme A Dehydrogenase Deficiency. In M. P. Adam (Eds.) et. al., GeneReviews®. University of Washington, Seattle.