

Molecular Test for Medium-Chain Acyl-CoA Dehydrogenase Deficiency

The UNC Hospitals' Molecular Genetics Laboratory performs DNA analysis to detect the K329E and Y42H mutations in the ACADM gene associated with medium-chain acyl-CoA dehydrogenase deficiency (MCADD).

Clinical and Molecular Features: MCADD is an autosomal recessive inborn error of fatty acid metabolism most common in Caucasians of Northern European descent. Medium chain acyl-CoA dehydrogenase is involved in mitochondrial fatty acid β -oxidation. Patients with MCADD are unable to utilize stored fat for energy during periods of prolonged fasting or high-energy demand, for example during illness. MCADD has been part of the newborn screening protocol in the state of North Carolina since August of 1977. Patients with MCADD are typically normal at birth and by two years of age present with hypoketotic hypoglycemia, vomiting, lethargy, seizure, coma, or sudden death. There is significant phenotypic heterogeneity. Laboratory diagnosis is based on a number of biochemical analyses including plasma acylcarnitines, plasma-free fatty acids, and urine organic acids, and molecular genetic testing. Approximately 80% of affected patients are homozygous for the K329E mutation in the ACADM gene and an additional 18% are heterozygous for this mutation in combination with any of over 20 other rare alleles, of which Y42H is the most common. Asymptomatic parents and siblings of an affected individual may have reduced levels of medium chain acyl-CoA dehydrogenase activity and are candidates for genetic counseling and testing. Treatment for MCADD is quite effective and involves avoiding prolonged fasts and monitoring blood sugar levels during illness.

Laboratory Testing for the K329E and Y42H Mutations: The preferred sample is ACD anticoagulated blood (pale yellow top), which may be refrigerated up to 48 hours before analysis. PCR followed by pyrosequencing is used to detect the point mutations A985G that results in K329E and T199C that results in Y42H amino acid substitutions in the MCADD gene. Results are reported as heterozygous, homozygous, or normal.

References:

1. Online Mendelian Inheritance in Man: <http://www3.ncbi.nlm.nih.gov/htbin-post/Omim/dispim?201450>
2. Roe CR and Ding J. Mitochondrial Fatty Acid Oxidation Disorders. In: Scriver CR, Beaudet AL, Sly WS, et al., eds. The Metabolic and Molecular Bases of Inherited Disease, Eighth Edition. Volume 2. New York:McGraw-Hill, 2001:2297-2326.
3. Gene Reviews: <http://www.geneclinics.org>

Questions? Call the UNC Molecular Genetics Lab at (919) 966-4408 or Dr. Jessica Booker at (919) 966-7894

E-mail: jbooker@unch.unc.edu

Website: http://labs.unchealthcare.org/directory/molecular_pathology/index_html