Medium Chain Acyl Co-A Dehydrogenase (MCADD): \textit{ACADM} Gene Deletion/Duplication

\textbf{Test Code: DACAD}

\textbf{Turnaround time:} 2 weeks

\textbf{CPT Codes:} 81228 x1

\section*{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 2 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 (\textit{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 \textit{ACADM} is recommended for patients with a biochemical diagnosis of MCADD as a complementary method to confirm the presence of mutations in a proband, identify carriers among the probands relatives, and provide prenatal diagnosis in families with known mutations. Sequencing is recommended only after mutation analysis for the \textit{K304E} and \textit{Y42H} mutations has been performed.

Reference:

\section*{Genes}

\textbf{ACADM}

\section*{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 or no mutations identified through the common mutation panel.

\section*{Methodology}

DNA isolated from peripheral blood is hybridized to a CGH array to detect deletions and duplications. The targeted CGH array has overlapping probes which cover the entire genomic region.

Please note that a "backbone" of probes across the entire genome are included on the array for analytical and quality control purposes. Rarely, off-target copy number variants causative of disease may be identified that may or may not be related to the patient's phenotype. Only known pathogenic off-target copy number variants will be reported. Off-target copy number variants of unknown clinical significance will not be reported.

\section*{Detection}

Detection is limited to duplications and deletions. The CGH array will not detect point or intronic mutations.

Results of molecular analysis must be interpreted in the context of the patient's clinical and/or biochemical phenotype.

\section*{Specimen Requirements}

Submit only 1 of the following specimen types

* Preferred specimen type: Whole Blood

\textbf{Type: Whole Blood}

Specimen Requirements:

In EDTA (purple top) or ACD (yellow top) tube:
- Infants (2 years): 3-5 ml
- Older Children & Adults: 5-10 ml

Specimen Collection and Shipping: Refrigerate until time of shipment. Ship sample within 5 days of collection at room temperature with overnight delivery.

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**Type: Saliva**

Specimen Requirements:

Oragene™ Saliva Collection kit (available through EGL) used according to manufacturer instructions.

Specimen Collection and Shipping: Store sample at room temperature. Ship sample within 5 days of collection at room temperature with overnight delivery.

**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 Profile (PA) - Plasma 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.
- Known Mutation Analysis (KM) is available to family members if mutations are identified by sequencing.
- 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.