ACAD9 Deficiency: ACAD9 Gene Deletion/Duplication

Test Code: DACA9  
Turnaround time: 2 weeks  
CPT Codes: 81228 x1

Condition Description

In 2007, He et al. reported three cases of acyl-CoA dehydrogenase 9 (ACAD9) deficiency. The three cases presented with episodic liver dysfunction during otherwise mild illness or cardiomyopathy, along with chronic neurologic dysfunction.

The first affected individual was a previously healthy 14-year-old boy who died of a Reye-like episode and cerebellar stroke triggered by ingestion of aspirin during a minor viral illness. He had markedly elevated plasma ammonia concentration and elevated results from liver function tests. Also elevated were serum salicylate levels, serum lactate levels, lactate dehydrogenase levels, and creatine kinase levels.

The second affected individual was a 10-year-old girl who initially presented with fulminant liver failure at age 4 months. Her blood glucose level at time of presentation was not detectable and AST was >100,000 U/liter. She responded well to intravenous glucose therapy, but continued to have recurrent episodes of hepatocellular dysfunction with hypoglycemia usually triggered by viral infections.

The third affected individual was a 4.5-year-old girl who died of cardiomyopathy and dilated left ventricle. Her sibling also died of cardiomyopathy at age 22 months. She presented during an episode of acute illness at age 18 months with severe left ventricular dysfunction, hepatomegaly, and a blood glucose level <20 mg/dl. She then developed a pattern of recurrent rhabdomyolysis with intercurrent illness. She died of congestive heart failure at age 4.5 years, and autopsy revealed dilated cardiomyopathy with prominent liver necrosis.

Mutations in the ACAD9 gene (3q26) cause ACAD9 deficiency.

For patients with suspected ACAD9 deficiency, sequence analysis is recommended as the first step in mutation identification. For patients in whom mutations are not identified by full gene sequencing, deletion/duplication analysis is appropriate.

References:

Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of ACAD9 deficiency in individuals who have tested negative for sequence analysis
- Carrier testing in adults with a family history of ACAD9 deficiency who have tested negative for sequence analysis

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.

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.

Specimen Requirements

Submit only 1 of the following specimen types

* Preferred specimen type: Whole Blood

Type: Whole Blood

Specimen Requirements:

In EDTA (purple top) tube:
- Infants (2 years): 3-5 ml
- Older Children & Adults: 5-10 ml
Specimen Collection and Shipping: Ship sample at room temperature with overnight delivery.

**Special Instructions**

Submit copies of diagnostic biochemical test results with the sample, if appropriate. 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 Emory Genetics Laboratory, please submit a copy of the sequencing report with the test requisition.

**Related Tests**

- Sequence analysis of the ACAD9 gene is available and is required before deletion/duplication analysis.
- 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.