MEDIUM CHAIN ACYL CoA DEHYDROGENASE DEFICIENCY (MCAD)

London Health Sciences Centre | St JOSEPH'S HEALTH CARE LONDON

Pathology and Laboratory Medicine

Orderable - MD MCAD Screen

Turnaround Time: 4-6 weeks **STAT: 4 weeks**

Laboratory:
Molecular Diagnostics Lab

Requisition:
MOLECULAR DIAGNOSTICS REQUISITION

Method of Analysis:
All coding exons and 20 bp of flanking intronic sequence are enriched using an LHSC custom targeted hybridization protocol (Roche Nimblegen), followed by high throughput sequencing (Illumina). Sequence variants and copy number changes are assessed and interpreted using clinically validated algorithms and commercial software (SoftGenetics: Nextgene, Geneticist Assistant, Mutation Surveyor; and Alamut Visual). All exons have >300x mean read depth coverage, with a minimum 100x coverage at a single nucleotide resolution. This assay meets the sensitivity and specificity of combined Sanger sequencing and

Alternate Name(s):

ACADM
MCAD

Specimen:

Whole blood-2 x 4 mL Lavender EDTA top Vacutainer tube

Collection Information:

Sample may be transported at room temperature

Reference Ranges:

See report

Interpretive Comments:

Medium chain acyl CoA dehydrogenase (ACADM, a.k.a. MCAD) deficiency is a recessive trait associated with defective oxidation of fatty acids which may have serious clinical sequelae. In the Ontario population approximately 90% (PMID:20434380) of alleles associated with ACADM (MCAD) deficiency have a single A>G mutation at nucleotide #985. Thus approximately 81% of clinically affected members of this population would be expected to be homozygous for the 985A>G mutation, 18% would be compound heterozygotes while 13% of the alleles are expected to carry the 199C>T mutation with the remaining mutations being private mutations distributed throughout the ACADM gene.

Comments:

Full ACADM gene sequencing and del/dup analysis.

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Storage and Shipment:

Store and ship at room temperature within 5 days of collection.

MLPA copy number analysis. All variants interpreted as either ACMG category 1, 2, or 3 (pathogenic, likely pathogenic, VUS; PMID: 25741868) are confirmed using Sanger sequencing, MLPA, or other assays. ACMG category 4 and 5 variants (likely benign, benign) are not reported, but are available upon request. This assay has been validated at a level of sensitivity equivalent to the Sanger sequencing and standard copy number analysis (>99%; PMID: 27376475).

Test Schedule:
As required,
Monday to Friday 0800-1600 hours