**ACSL4-related Disorders: ACSL4 Gene Deletion/Duplication**

**Condition Description**

Mutations in the ACSL4, also known as FACL4, gene (Xq22.3) have been associated with severe non-syndromic X-linked intellectual disability. Affected males show nonspecific, nonprogressive intellectual disability, ranging from severe to moderate without seizures, whereas carrier females showed highly variable cognitive capacities, ranging from moderate intellectual disability to normal intelligence. ACSL4 deletions have also been found in patients with Alport syndrome, elliptocytosis, and intellectual disability.

Long chain acyl-CoA synthetase (LACS) or long chain fatty acid-CoA ligase (FACL) converts free long chain fatty acids into fatty acyl-CoA esters, which are key intermediates in the synthesis of complex lipids. The ACSL4 gene encodes a form of LACS and is expressed in several tissues, including the brain. Both point mutations and deletions have been reported in the gene. Reduction of FACL4 activity may lead to deranged fatty acid metabolism in neurons, causing defects of neuron outgrowth, synaptogenesis, and other developmental functions important for normal brain development.

For patients with a suspected ACSL4-related disorder, 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.

**Genes**

**ACSL4**

**Indications**

This test is indicated for:

- Confirmation of a clinical/biochemical diagnosis of an ACSL4/FACL4-related disorder.
- Carrier testing in adult females with a family history of an ACSL4/FACL4-related disorder.

**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.

**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: Refrigerate until time of shipment. Ship sample within 5 days of collection at room temperature with overnight delivery.

**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

Related Tests

- Sequence analysis of the ACSL4 gene is available and is required before deletion/duplication analysis.
- An X-Linked Intellectual Disability panel with sequencing and deletion/duplication analysis is available for 110 genes.
- Known Mutation Analysis (KM) is available to family members if mutations are identified by targeted mutation testing or sequencing analysis.
- Prenatal Custom Diagnostics is available to adult females who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.