Allan-Herndon-Dudley Syndrome: SLC16A2 Gene Deletion/Duplication

Test Code: YG
Turnaround time: 2 weeks
CPT Codes: 81404 x1

Condition Description

Allan-Herndon-Dudley syndrome is an X-linked recessive disorder caused by mutations in the SLC16A2 (also called MCT8) gene (Xq13.2). Common characteristics of this disorder include moderate to severe mental retardation, impaired speech, hypotonia, muscle weakness, and contractures. Symptoms seen in infancy and childhood can consist of hypotonia, weakness, reduced muscle mass, and delay of developmental milestones. Facial characteristics are not distinctive, but the face tends to be elongated with bifrontal narrowing, and the ears are often simply formed or cupped. Some patients have myopathic facies. Generalized weakness is manifested by excessive drooling, forward positioning of the head and neck, failure to walk independently, or ataxia in those who do walk. Speech is dysarthric or absent altogether.

Hypotonia gives way in adult life to spasticity. The hands exhibit dystonic and writhing posturing and fisting. Cognitive development is severely impaired. No major malformations occur and head circumference and genital development are usually normal. Behavior tends to be passive, with little evidence of aggressive or disruptive behavior.

Mutations in the SLC16A2 gene impair thyroid hormone transport. Although clinical signs of thyroid dysfunction are usually absent in affected males, the disturbances in blood levels of thyroid hormones can be seen, such as increased serum T3 levels. Some female carriers may have mild serum thyroid hormone abnormalities but no neurologic manifestations. Both point mutations and partial gene deletions have been reported in this gene.

For patients with suspected Allan-Herndon-Dudley syndrome, 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

MCT8, SLC16A2

Indications

This test is indicated for:
- Confirmation of a clinical diagnosis of Allan-Herndon-Dudley syndrome in individuals who have tested negative for sequence analysis
- Carrier testing in adult females with a family history of Allan-Herndon-Dudley syndrome 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: Refrigerate until time of shipment. Ship sample within 5 days of collection at room temperature with overnight delivery.

Type: Saliva

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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
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 EGL Genetics, please submit a copy of the sequencing report with the test requisition.

Related Tests
- Sequencing analysis of the SLC16A2 gene is available (YF) and is required before deletion/duplication analysis.
- X-Linked Intellectual Disability panels are available for 30, 60, and 90+ genes.
- Prenatal testing 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.