Danon Disease: LAMP2 Gene Deletion/Duplication

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

Condition Description

Danon Disease is an X-linked disorder that can affect cardiac muscle, skeletal muscle, and mental retardation. Affected individuals have also been described with hypertrophic cardiomyopathy, proximal muscle weakness, hepatomegaly, peripheral pigmentary retinopathy, and elevated creatine kinase. Presentation can be variable even within a family. Affected individuals usually die in their teens or twenties due to heart failure; heart transplantation has been shown to be an effective treatment. Females have been reported to display symptoms of Danon disease, as well. Symptoms reported in affected females include skeletal myopathy, atrial fibrillation, mild left ventricular enlargement with systolic dysfunction on echocardiogram, pigmentary retinopathy, mild intellectual impairment, mental retardation, and death from cardiac disease. While cardiomyopathy in affected males occurs before the age of 20, most affected females develop cardiomyopathy in adulthood.

Mutations in the LAMP2 gene (Xq24) have been associated with Danon disease. One study reported that the prevalence of Danon disease was 1% of patients with hypertrophic cardiomyopathy (2 of 197 patients). In this study, Danon disease was responsible for 50% of the cases of hypertrophic cardiomyopathy (CMH) with clinical skeletal myopathy (2 of 4 patients); none of the 41 patients with isolated CMH had Danon disease. In another study, genetic analyses of 24 subjects with increased left ventricular wall thickness and electrocardiogram suggesting ventricular preexcitation found 4 LAMP2 mutations. Clinical features associated with defects in LAMP2 included male sex, severe hypertrophy, early onset (at 8 to 17 years of age), ventricular preexcitation, and asymptomatic elevations of two serum proteins. Mutations in heterozygous state appeared to be responsible for unusual heart disease in some females.

Although this disorder was originally described as a variant of glycogen storage disease II due to accumulation of glycogen in muscle and lysosomes seen in some patients, acid alpha-glucosidase and other enzymes of glycogen metabolism are normal. Glycogen, however, is not always increased in affected individuals. The subsequent identification of the structural lysosome-associated membrane protein-2 gene as responsible for the disorder enabled the proper identification of Danon disease as resulting from a defect of the lysosomal membrane.

Click here for the OMIM summary on this condition.

Genes

LAMP2

Indications

This test is indicated for:

- Confirmation of a clinical/biochemical diagnosis of Danon disease in individuals who have tested negative for sequence analysis
- Carrier testing in adult females with a family history of Danon disease 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) 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.

**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**

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 LAMP2 gene is available 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.