

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.

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

Type: Whole Blood (EDTA)

Specimen Requirements:

EDTA (Purple Top)

Infants and Young Children (2 years of age to 10 years old): 3-5 ml

Older Children & Adults: 5-10 ml

Autopsy: 2-3 ml unclotted cord or cardiac blood

Specimen Collection and Shipping:

Ship sample at room temperature for receipt at EGL within 72 hours of collection. Do not freeze.

Type: DNA, Isolated

Specimen Requirements:

Microtainer

3µg

Isolation using the Perkin Elmer™ Chemagen™ Chemagen™ Automated Extraction method or Qiagen™ Puregene kit for DNA extraction is

recommended.

Specimen Collection and Shipping:

Refrigerate until time of shipment in 100 ng/ μ L in TE buffer. 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 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.