Fabry Disease: GLA Gene Deletion/Duplication

**Test Code:** KX  
**Turnaround time:** 2 weeks  
**CPT Codes:** 81228 x1

**Condition Description**

Fabry disease is an X-linked condition caused by a deficiency of alpha-galactosidase A enzyme activity. Affected individuals are unable to metabolize globotriaosylceramide (GL-3) in their lysosomes. The progressive accumulation of GL-3 results in symptoms that include:

- characteristic lysosomal disease skin rashes (angiokeratomas)
- decreased sweating (hypohidrosis)
- chronic fatigue
- depression
- neuropathic pain in the hands and feet (acroparesthesia)
- gastrointestinal issues
- strokes
- cardiac disease (including left ventricular hypertrophy)
- renal disease (proteinuria to end stage renal disease)

The diagnosis of Fabry disease has increased in importance since treatment with enzyme replacement therapy is now available.

Fabry disease affects both men (hemizygotes) and women (heterozygotes), however, the testing strategy varies based on gender. Alpha galactosidase A enzyme analysis alone will detect nearly all affected males and approximately 60% of heterozygous females with Fabry disease. Combining enzyme analysis with sequencing of the alpha galactosidase A gene increases the speed and reliability of testing females for Fabry disease. Alpha galactosidase A enzyme analysis can be performed on samples concurrently with gene sequencing. Sequencing is available for males with a biochemical diagnosis of Fabry. The Fabry Testing Roadmap is available to help choose the correct tests for diagnosis of Fabry disease in males or females.

Mutations to the GLA gene, located at Xq22, result in a deficiency of the enzyme alpha-galactosidase A. Most mutations are familial, however, a few de novo mutations have been reported.

For further information about lysosomal storage diseases, please call the Emory Lysosomal Storage Disease Center at (404)778-8565 or (800)200-1524. For general questions, call EGL Genetics at (404)778-8500.

Please click here for the GeneReviews summary on this condition.


**Genes**

**GLA**

**Indications**

This test is indicated for:

- Patients with a confirmed or suspected diagnosis of Fabry disease.
- Family members of a person diagnosed with Fabry disease.

**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

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Specimen Collection and Shipping:
Ship sample at room temperature for receipt at EGL within 24 hours of collection. Do not refrigerate or 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/µL in TE buffer. Ship sample at room temperature with overnight delivery.

Special Instructions

Please submit copies of diagnostic biochemical test results along with the sample. 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

- Alpha-Galactosidase A Enzyme Activity (LB).
- Known Mutation Analysis (KM) is available to family members if mutations are identified by sequencing.
- Prenatal Custom Diagnostics is available to couples who are carriers of GLA gene mutations. Please contact the laboratory genetic counselor to arrange prior to collecting a prenatal specimen. Sequencing is not appropriate for prenatal samples in which familial mutations have not been identified.