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 Emory Genetics Laboratory 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.

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**

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 Emory Genetics Laboratory, 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.