GLA Gene Sequencing Assay (Fabry Disease): Test Ordering Information

Test Information: (06202012_v1)

GLA Gene Sequencing Assay (Fabry Disease) (CMGDL test code 3003)

For additional information please refer to the CMGDL www.medgen.med.miami.edu.

Indications for Testing
-to confirm or establish a Fabry disease diagnosis in male patients, generally after α-galactosidase (α-Gal A) enzyme activity has been determined;
-to confirm the carrier state in females with markedly decreased α-Gal A enzyme activity;
-to clarify the genetic carrier status in females with an α-Gal A enzyme activity in the normal range;
-to rule in an atypical Fabry disease diagnosis in patients with late onset of cardiomyopathies;
-to rule in an atypical Fabry disease diagnosis in patients on renal dialysis or undergoing renal transplantation without a primary or biopsy diagnosis for Fabry disease;

Note: this test is not designed to identify and detect the deep intronic gene mutations. Please contact us for further information.

Contraindications
-Testing should not be ordered for individuals with previously identified familial GLA mutations. To test for a specific mutation, it is recommended to order Family Testing, Gene Sequencing Targeted Mutation Analysis (CMGDL test code 3000) and provide a copy of the laboratory report stating the familial mutation.
-Prenatal testing is not performed by the CMGDL.

Specimen Requirements
2.0 ml of whole blood (minimum)
Collection Tube: Lavender Top Tube /w EDTA
Handling: Room Temp- specimen processed within 72 hours

Turn-Around Times
21 to 28 business days
(see www.medgen.med.miami.edu/ for eventual TAT changes or updates)

Methodology and Assay Characteristics
This test is performed by using the Sanger’s method, which is also referred to as dideoxy sequencing or chain termination sequencing. Briefly, genomic DNA segments of 100-500 nucleotides (in general containing the gene exons of interest plus an additional 20 base pairs from the exon/intron junction into the intron) are enriched by polymerase chain reaction (PCR). The products of this amplification reaction are then sequenced bi-directionally.

Clinical Sensitivity
In males, nearly 100% of affected patients have a mutation identifiable by gene sequencing of the GLA gene, the only gene known to be associated with Fabry disease.

Analytical Sensitivity and Specificity
99 percent of analytical sensitivity and specificity.

Test Limitations
(see www.medgen.med.miami.edu/ for additional information)
-Gene sequencing by Sanger’s method cannot detect large deletions as well as it cannot detect other genomic rearrangements;
-Gene sequencing tests may reveal or suggest non-paternity in certain cases;
-This method is affected by allele-dropout, although this phenomenon is minimized by the selection of primer binding sites not containing known variants. If the allele-dropout occurs, only one allele of two will be amplified: in this case eventual variants on the dropped allele will not be detected and eventual variants located on the amplified allele may be falsely detected as homozygous;
-This test is designed to detect all the gene exons and around 20 nucleotides into the intronic regions; mutations that occur outside of these regions would not be detected;
-Clinical molecular genetics is a fast-moving field. The gene variant interpretation may change as new medical and scientific information becomes available;
-Results of this test should be interpreted in the context of the clinical presentation and in consultation with a clinical geneticist.

This test was developed and its performance determined by the CMGDL. The CMGDL has clinically validated it and determined its accuracy and precision. It has not been cleared or approved by the U.S. Food and Drug Administration. This test is used for clinical purposes. Pursuant to the requirements of CLIA ’88, this laboratory has verified the test accuracy and precision. Genetic testing using the methods applied by the CMGDL is
expected to be highly accurate. However, the chance of a false positive or a false negative result, due to laboratory errors incurred during any phase of the testing, cannot be completely excluded.

References
- OMIM. Fabry Disease. # 301500. http://www.omim.org/entry/301500

Related Tests
- Family Testing, Gene Sequencing Targeted Mutation Analysis (test code 3000) (visit our website at www.medgen.med.miami.edu)