Pompe Disease: GAA Gene Deletion/Duplication

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

**Condition Description**

Glycogen storage disease type II (GSD-II) is an autosomal recessive disorder due to a deficiency of the lysosomal enzyme acid alpha-1,4-glucosidase (abbreviated GAA). The function of the GAA enzyme, also known as acid maltase, is to breakdown glycogen in the lysosome. Absent or reduced GAA activity results in accumulation of glycogen within the lysosome, particularly in muscle cells. GSD-II is divided into two forms; an infantile form and a juvenile/adult onset form. In individuals with the infantile form of Pompe disease there is less than 1% of normal enzymatic activity, whereas in the juvenile/adult onset form there is some residual enzymatic activity. In Pompe disease, affected infants are severely hypotonic and have cardiomegaly. In addition, patients may have an enlarged tongue. The disease is usually fatal within the first year of life due cardiorespiratory failure. The clinical presentation in the juvenile/adult onset form (onset after 12 months of age) is much more variable than in the Infantile form of Pompe disease. In this later onset form of the disease, patients generally suffer from slowly progressive proximal muscle weakness with progressive respiratory insufficiency. Unlike the infantile form, in the later onset form there is usually not cardiomegaly or cardiomyopathy.

Mutations in the GAA gene cause deficiency of the GAA enzyme. More than 200 mutations in the GAA gene have been described to date[1]. The most common variant found in GSD II is a change in intron 1, specifically a splice site mutation, that is associated with the late onset form of the disease[2]. The life expectancy of these patients varies considerably, with death ultimately occurring due to respiratory insufficiency. Enzyme replacement therapy for treatment of symptoms of Pompe disease is FDA approved.

For questions about testing for Pompe disease, call EGL Genetics at (470) 378-2200 or (855) 831-7447. For further clinical information about lysosomal storage diseases, including management and treatment, call the Emory Lysosomal Storage Disease Center at (404) 778-8565 or (800) 200-1524.


**References:**
1). www2.eur.nl/fgg/ch1/pompe  

**Genes**

**GAA**

**Indications**

- Confirmation of a clinical diagnosis of GSD II  
- Prenatal testing for known familial mutations.  
- Assessment of carrier status in high risk family members known mutation 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. Array CGH will not detect point mutations 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) 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. Sequence analysis is required before deletion/duplication analysis by targeted CGH array. If sequencing is performed outside EGL Genetics, please submit a copy of the sequencing report with the test requisition. Contact the laboratory if further information is needed.

**Related Tests**

- Known Mutation Analysis (KM) is available to test family members.
- Prenatal testing is available for known familial mutations only. Please call the Laboratory Genetic Counselor for specific requirements for prenatal testing before collecting a fetal sample.