Pompe Disease

Gene Tested: *GAA*

Also Known As:

- Glycogen storage disease type II (GSD-II)
- Acid maltase deficiency (AMD)

Disorder: Pompe disease is a lysosomal storage disease and is caused by a deficiency of acid alpha-glucosidase (GAA). Pompe disease is inherited as an autosomal recessive disorder. Most sources say there are two types of Pompe disease: infantile onset and later onset. In the infantile-onset form of Pompe disease, the earliest symptoms occur in the first weeks of life. In the later onset form, the first symptoms occur in childhood or early adulthood. It is estimated that about 1 in every 140,000 newborns has infantile onset Pompe disease. The later onset form of Pompe disease is more common, with 1 in every 60,000 people affected.

Newborns with infantile Pompe disease often do not show signs of the condition. Within the first months of life, parents may notice feeding problems, irritability, poor head control, and a protruding tongue. The child may also have hypotonia and absent reflexes, respiratory distress and/or hepatomegaly. A chest X-ray, echocardiogram, or electrocardiogram may show an enlarged heart consistent with hypertrophic cardiomyopathy. The disease is progressive and usually fatal in the first year of life.

A person with later onset Pompe disease does not show symptoms of the condition at birth. As children, individuals with later onset Pompe disease may seem clumsy, have decreased stamina, or have difficulty performing certain activities, such as sit-ups. The disease is often not diagnosed, however, until individuals have more severe symptoms including lower extremity and truncal muscle weakness, resulting in decreased ambulation, shortness of breath, scoliosis, and back pain.

Pompe disease can be confirmed by documenting absent or deficient acid alpha-glucosidase (GAA) in skin fibroblasts or by documenting the presence of two mutations in the *GAA* gene.

Indications:

- Confirmation of diagnosis in a symptomatic individual
- Presymptomatic testing of at-risk relatives
- Carrier identification in individuals with a family history of Pompe disease
- Prenatal diagnosis of an at-risk fetus, after confirmation of mutations in the parents (by prior arrangement only)

Specimen:

Blood samples should be collected in EDTA (lavender topped) tubes. A minimum of 5 mLs on adult or 3 mLs on child is required for analysis. Blood collected on Friday may be stored in refrigerator until Monday for overnight shipment.

For other tissue requirements please call 1-800-344-2462, extension 4474.

Testing Methodology: PCR-based sequencing of all 20 exons and exon/intron boundaries of the *GAA* gene. Testing also includes PCR-fragment length analysis of exon 18.

Test Sensitivity:

PCR-based sequencing detects two mutations in ~ 90% of patients with infantile onset Pompe disease and in ~80% of patients with later juvenile and adult onset forms. The sensitivity of DNA sequencing is over 99% for the detection of nucleotide base changes, small deletions and insertions in the regions analyzed. Deletion of exon 18 is seen in approximately 5-7% of Pompe alleles and is detected by PCR fragment analysis in the vast majority of cases. Deletions of other exon(s) have been reported as well and are not detected by this test methodology. *GAA* is the only gene associated with Pompe disease.

Cincinnati Children's
Human Genetics

Molecular Genetics Laboratory
CLIA#: 36D0656333
Phone: (513) 636-4474
Fax: (513) 636-4373
Email: moleculargenetics@cchmc.org
www.cincinnatichildrens.org/molecular-genetics

Turn-Around Time: Reports are routinely available within 21 days of sample receipt. Sequencing for infantile Pompe disease will be completed in 7 days. **Please note that the charge for infantile Pompe disease sequencing is greater than the charge for general sequencing.** Abnormal results will be called to the referring physician. All reports will be faxed to the referring physician.

CPT Codes:

- Infantile Pompe Full Gene *(GAA)* Sequencing 81406
- Pompe Full Gene *(GAA)* Sequencing 81406
- Family Mutation Studies 81403

Please call 1-866-450-4198 for pricing, insurance preauthorization, or with any billing questions.

Results: Each test report includes a detailed interpretation of the genetic findings, the clinical significance of the result, and specific recommendations for clinical management and additional testing, if warranted. Results will be reported to the referring physician or health care provider as specified on the test requisition form.

Additional information and test requisitions are available at: www.cchmc.org/molecular-genetics

Shipping Instructions:

Please enclose **test requisition** with sample.
All information must be completed before sample can be processed.

Place samples in styrofoam mailer and ship at room temperature by overnight Federal Express to arrive Monday through Friday

Ship to:

Cytogenetics and Molecular Genetics Laboratories
3333 Burnet Avenue NRB 1042
Cincinnati, OH 45229
513-636-4474