MAYO CLINIC LABORATORIES

Test Definition: GAAZ

Pompe Disease, Full Gene Analysis, Varies

Overview

Useful For

Confirmation of diagnosis of Pompe disease (as a follow-up to biochemical analyses)

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
CULFB	Fibroblast Culture for Genetic Test	Yes	No

Testing Algorithm

For skin biopsy or cultured fibroblast specimens, fibroblast culture testing will be performed at an additional charge. If viable cells are not obtained, the client will be notified.

For more information see:
-Newborn Screen Follow-up for Pompe Disease

Special Instructions

- Molecular Genetics: Congenital Inherited Diseases Patient Information
- Informed Consent for Genetic Testing
- Blood Spot Collection Card-Spanish Instructions
- Newborn Screen Follow-up for Pompe Disease
- Blood Spot Collection Card-Chinese Instructions
- Informed Consent for Genetic Testing (Spanish)
- Blood Spot Collection Instructions

Method Name

Polymerase Chain Reaction (PCR) followed by DNA Sequencing

NY State Available

Yes

Specimen

Specimen Type

Varies

Ordering Guidance

For first tier testing for individuals older than 6 weeks with a suspected diagnosis of Pompe disease, order PDBS / Pompe Disease, Blood Spot. If the patient is 6 weeks old or younger, order PD2T / Pompe Disease Second-Tier Newborn

Screening, Blood Spot.

Alternatively, enzyme studies can be performed on whole blood; order GAAW / Acid Alpha-Glucosidase, Leukocytes.

For measurement of ongoing therapeutic monitoring, order HEX4 / Glucotetrasaccharides, Random, Urine.

Shipping Instructions

Specimen preferred to arrive within 96 hours of collection.

Specimen Required

Patient Preparation: A previous bone marrow transplant from an allogenic donor will interfere with testing. Call 800-533-1740 for instructions for testing patients who have received a bone marrow transplant.

Submit only 1 of the following specimens:

Preferred:
Specimen Type: Whole blood
Container/Tube:
Preferred: Lavender top (EDTA) or yellow top (ACD)
Acceptable: Any anticoagulant
Specimen Volume: 3 mL
Collection Instructions:
1. Invert several times to mix blood.
2. Send whole blood specimen in original tube. **Do not aliquot.**
Specimen Stability Information: Ambient (preferred)/Refrigerated

Specimen Type: Cultured fibroblasts
Container/Tube: T-75 or T-25 flask
Specimen Volume: 1 Full T-75 or 2 full T-25 flasks
Specimen Stability Information: Ambient (preferred)/Refrigerated 24 hours
Additional Information: A separate culture charge will be assessed under CULFB / Fibroblast Culture for Biochemical or Molecular Testing. An additional 3 to 4 weeks is required to culture fibroblasts before genetic testing can occur.

Specimen Type: Skin biopsy
Supplies: Fibroblast Biopsy Transport Media (T115)
Container/Tube: Sterile container with any standard cell culture media (eg, minimal essential media, RPMI 1640). The solution should be supplemented with 1% penicillin and streptomycin.
Specimen Volume: 4-mm punch
Specimen Stability Information: Refrigerated (preferred)/Ambient
Additional Information: A separate culture charge will be assessed under CULFB / Fibroblast Culture for Biochemical or Molecular Testing. An additional 3 to 4 weeks is required to culture fibroblasts before genetic testing can occur.

Specimen Type: Blood spot
Supplies: Card - Blood Spot Collection (Filter Paper) (T493)
Container/Tube:
Preferred: Collection card (Whatman Protein Saver 903 Paper)

Acceptable: PerkinElmer 226 (formerly Ahlstrom 226) filter paper or blood spot collection card
Specimen Volume: 2 to 5 Blood spots on collection card
Collection Instructions:
1. An alternative blood collection option for a patient older than 1 year is a fingerstick. For detailed instructions, see How to Collect Dried Blood Spot Samples.
2. Let blood dry on the filter paper at ambient temperature in a horizontal position for a minimum of 3 hours.3. Do not expose specimen to heat or direct sunlight.
4. Do not stack wet specimens.
5. Keep specimen dry
Specimen Stability Information: Ambient (preferred)/Refrigerated
Additional Information:
1. Due to lower concentration of DNA yielded from blood spot, it is possible that additional specimen may be required to complete testing.
2. For collection instructions, see Blood Spot Collection Instructions
3. For collection instructions in Spanish, see Blood Spot Collection Card-Spanish Instructions (T777)
4. For collection instructions in Chinese, see Blood Spot Collection Card-Chinese Instructions (T800)

Forms

1. **New York Clients-Informed consent is required**. Document on the request form or electronic order that a copy is on file. The following documents are available in Special Instructions:
-Informed Consent for Genetic Testing (T576)
-Informed Consent for Genetic Testing-Spanish (T826)
2. Molecular Genetics: Congenital Inherited Diseases Patient Information (T521) in Special Instructions
3. If not ordering electronically, complete, print, and send a Biochemical Genetics Test Request (T798) with the specimen.

Specimen Minimum Volume

Blood: 1 mL
Blood Spots: 5 punches-3 mm diameter

Reject Due To

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Varies		

Clinical & Interpretive

Clinical Information

Pompe disease, also known as glycogen storage disease type II, is an autosomal recessive condition caused by deficiency of acid alpha-glucosidase. Enzyme insufficiency results in symptoms such as muscle weakness, cardiomyopathy, and respiratory problems. Pathogenic alterations in the *GAA* gene (which encodes acid alpha-glucosidase) are associated with Pompe disease.

The diagnosis of this heterogeneous condition relies on both clinical and laboratory evaluation. Clinically, the condition is categorized into infantile and late-onset forms based on age of onset, organ involvement, and rate of progression. The infantile form (or classic Pompe disease) is the most severe form and is characterized by early onset and rapid progression of cardiac, liver, and muscle problems resulting in death within the first year. The infantile variant form has a similar age of onset but a milder clinical presentation. On the less severe end of the spectrum is the late-onset form with childhood, juvenile, or adult onset. The rate of progression and severity of symptoms is quite variable, particularly in the late-onset forms. The incidence varies by clinical type and ethnic population; the combined incidence is approximately 1 in 40,000 individuals.

The calculated ratio of creatine (Cre) and creatinine (Crn) to acid-alpha glucosidase (GAA) activity is useful for individuals with a suspected diagnosis of Pompe disease; for patients older than 6 weeks, order PDBS / Pompe Disease, Blood Spot; for patients 6 weeks and younger, order PD2T / Pompe Disease Second-Tier Newborn Screening, Blood Spot. Alternatively, enzyme studies can be ordered on blood via GAAW / Acid Alpha-Glucosidase, Leukocytes. When clinical manifestations and results of that analysis are supportive of a diagnosis of Pompe disease, variant analysis of the *GAA* gene is warranted. Additionally, measurement of the urine glucotetrasaccharide biomarker can aid in diagnosis and ongoing therapeutic monitoring (HEX4 / Glucotetrasaccharides, Random, Urine)

Over 250 different variants have been identified in this gene including point alterations and large deletions. *GAA* full gene sequencing provided by this test will detect 2 variants in approximately 83% to 93% of individuals with confirmed GAA enzyme deficiency. Identification of genetic variants provides confirmation of the diagnosis and allows for subsequent testing of at risk family members.

Reference Values

An interpretive report will be provided.

Interpretation

All detected alterations are evaluated according to American College of Medical Genetics and Genomics (ACMG) recommendations.(1) Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance.

Cautions

A small percentage of individuals who are carriers or have a diagnosis of Pompe disease may have a genetic variant that is not identified by this method (eg, large genomic deletions or duplications, promoter alterations). The absence of a variant, therefore, does not eliminate the possibility of positive carrier status or the diagnosis of Pompe disease. For carrier testing, it is important to first document the presence of a *GAA* gene variant in an affected family member.

In some cases, DNA alterations of undetermined significance may be identified.

Rare alterations exist that could lead to false-negative or false-positive results. If results obtained do not match the clinical findings, additional testing should be considered.

Test results should be interpreted in the context of clinical findings, family history, and other laboratory data. Errors in the interpretation of results may occur if information given is inaccurate or incomplete.

Clinical Reference

1. Richards S, Aziz N, Bale S, et al: Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. Genet Med. 2015 May;17(5):405-424
2. Kishnani PS, Steiner RD, Bali D, et al: Pompe disease diagnosis and management guideline. Genet Med. 2006 May;8(5):267-288
3. Van der Ploeg AT, Reuser AJJ: Pompe's disease. Lancet. 2008;372(9646):1342-1353
4. Kroos M, Pomponio RJ, van Vliet L, et al: Update of the Pompe disease mutation database with 107 sequence variants and a format for severity rating. Hum Mut. 2008;29(6):E13-26
5. Reuser AJJ, Hirschhorn R, Kroos MA: Pompe disease: Glycogen storage disease type II, acid a-glucosidase (acid maltase) deficiency. In**:** Valle DL, Antonarakis S, Ballabio A, Beaudet AL, Mitchell GA. eds. Online Metabolic and Molecular Bases of Inherited Disease. McGraw-Hill; 2019. Accessed June 30, 2020. Available at: https://ommbid.mhmedical.com/content.aspx?bookid=2709&sectionid=225890450

Performance

Method Description
Bidirectional sequence analysis is performed to test for the presence of a sequence variant in all coding regions and intron/exon boundaries of the *GAA* gene.(Unpublished Mayo method)

PDF Report
No

Day(s) Performed
Varies

Report Available
14 to 20 days

Specimen Retention Time
Whole Blood: 2 weeks (if available); Extracted DNA: 3 months

Performing Laboratory Location
Rochester

Fees & Codes

Fees
- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

81406-GAA (glucosidase, alpha; acid) (eg, glycogen storage disease type II [Pompe disease]), full gene sequence
88233-Tissue culture, skin or solid tissue biopsy (if appropriate)
88240-Cryopreservation (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
GAAZ	Pompe Disease Full Gene Analysis	76034-8

Result ID	Test Result Name	Result LOINC® Value
53915	Result Summary	50397-9
53916	Result	82939-0
53917	Interpretation	69047-9
53918	Additional Information	48767-8
53919	Specimen	31208-2
53920	Source	31208-2
53921	Released By	18771-6