MAYO CLINIC LABORATORIES

Test Definition: PDCRF

Pompe Disease CRIM Status, Fibro

Overview

Useful For

Determination of cross-reactive immunologic material status in patients with Pompe disease

Evaluating the best strategy for enzyme replacement therapy for patients with Pompe disease

Additional Tests

Test Id	Reporting Name	Available Separately	Always Performed
FIBR	Fibroblast Culture	Yes	Yes
CRYOB	Cryopreserve for Biochem Studies	No	Yes

Testing Algorithm

When this test is ordered, a fibroblast culture and cryopreservation for biochemical studies will always be performed at an additional charge. However, for multiple lysosomal enzyme assays on a patient utilizing fibroblast culture, only one culture is required regardless of the number of enzyme assays ordered. If viable cells are not obtained within 10 days, client will be notified.

See Newborn Screen Follow-up for Pompe Disease In Special Instructions

Special Instructions

- Biochemical Genetics Patient Information
- Newborn Screen Follow-up for Pompe Disease

Highlights

This test is used to determine cross-reactive immunological material (CRIM) status in patients with Pompe disease. CRIM status is important when assessing whether immunosuppression is needed when initiating enzyme replacement therapy for patients with Pompe disease.

Method Name

PDCRF: Western blot

CRYOB: Fibroblast Subculture followed by Cryopreservation and Storage

NY State Available

Yes

Specimen

Specimen Type

Tissue

Specimen Required

Submit only 1 of the following specimens:

Specimen Type: Cultured fibroblasts

Container/Tube: T-75 or T-25 flask

Specimen Volume: 1 Full T-75 flask or 2 full T-25 flasks

Specimen Stability Information: Ambient (preferred)/Refrigerated <24 hours
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

Forms

1. Biochemical Genetics Patient Information (T602) in Special Instructions.
2. If not ordering electronically, complete, print, and send a Biochemical Genetics Test Request (T798) with the specimen.

Reject Due To

Specimen in formalin or fixative preservative	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Tissue	Varies (preferred)		

Clinical & Interpretive

Clinical Information

Pompe disease, also known as glycogen storage disease type II, is an autosomal recessive disorder caused by a deficiency of the lysosomal enzyme acid alpha-glucosidase (GAA; acid maltase) due to alterations in the *GAA* gene. The estimated incidence is 1 in 40,000 live births. In Pompe disease, glycogen is taken up by lysosomes during physiologic cell turnover and accumulates, causing lysosomal swelling and cell damage, which results in organ dysfunction. Symptoms include progressive muscle weakness, cardiomyopathy, and, eventually, death if untreated.
Clinically, Pompe disease 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 variant and is characterized by early onset and rapid progression of cardiac, liver, and muscle problems resulting in death within the first year of life. The infantile variant of Pompe disease has a similar age of onset but a milder clinical presentation. Late-onset Pompe disease can present with muscle weakness, cardiomyopathy, and/or respiratory dysfunction in childhood or later, including advanced adulthood. The rate of progression and severity of symptoms is variable, particularly in the late-onset forms.
Treatment with enzyme replacement therapy (ERT) is available, making early diagnosis of Pompe disease desirable because early initiation of treatment improves the prognosis. Treatment with ERT can prolong survival in patients with infantile onset Pompe disease; however, the effectiveness of treatment is impacted by the presence or absence of cross-reactive immunologic material (CRIM) to the GAA enzyme. Patients who are CRIM-negative are more likely to develop antibodies against recombinant human GAA than patients who are CRIM-positive, thereby decreasing the effectiveness of treatment. Strategies to decrease the immune response to ERT, such as immunosuppression, rely on determination of CRIM status.
Molecular analysis of the *GAA* gene can determine CRIM status in over 90% of patients with Pompe disease (GAAZ / Pompe Disease, Full Gene Analysis, Varies). However, for those who have *GAA* variants that are not classified as either

CRIM-negative or -positive, CRIM testing in fibroblasts or leukocytes can determine final CRIM status. Therefore, CRIM testing is useful for either confirmation of CRIM status determined by molecular testing or determination of CRIM status if the genotype is not informative.

Reference Values
An interpretive report will be provided

Interpretation
The presence of cross-reactive immunologic material (CRIM) indicates a decreased likelihood that a patient affected with Pompe disease (acid alpha-glucosidase: GAA deficiency) will develop an immune response to enzyme replacement therapy with recombinant GAA.
The absence of CRIM in untreated patients with Pompe disease indicates a need to consider additional measures to prevent an immune response to the administration of enzyme replacement therapy with recombinant GAA.

Cautions
The test by itself is not diagnostic of Pompe disease, and results need to be interpreted in light of the clinical presentation and other laboratory tests, such as creatine kinase, acid alpha-glucosidase (GAA) activity, and GAA genotype.

Clinical Reference
1. Kishnani PS, Goldenberg PC, DeArmey SL, et al: Cross-reactive immunologic material status affects treatment outcomes in Pompe disease infants. Mol Genet Metab. 2010 Jan;99(1):26-33
2. Bali DS, Goldstein JL, Rehder C, et al: Clinical laboratory experience of blood CRIM testing in infantile Pompe disease.Mol Genet Metab Rep. 2015;5:76-79 doi: 10.1016/j.ymgmr.2015.10.012
3. Reuser AJ, Hirschhorn R, Kroos MA: Pompe disease: Glycogen storage disease type II, acid alpha-glucosidase (acid maltase) deficiency. In: Valle DL, Antonarakis S, Ballabio A, Beaudet AL, Mitchell GA. eds. The Online Metabolic and Molecular Bases of Inherited Disease. McGraw-Hill; 2019. Accessed May 25, 2021. Available at https://ommbid.mhmedical.com/content.aspx?bookid=2709&sectionid=225890450
4. Leslie N, Bailey L: Pompe disease. In: Adam MP, Ardinger HH, Pagon RA, et al, eds. GeneReviews [Internet]. University of Washington, Seattle; 2007. Updated May 11, 2017. Accessed May 25, 2021. Available at www.ncbi.nlm.nih.gov/books/NBK1261/

Performance

Method Description
Western blot analysis is performed using fibroblasts cultured from a skin biopsy. Lysed cells are quantitated for protein, separated by gel electrophoresis, and transferred to a polyvinylidene difluoride (PVDF) membrane. The PVDF membrane is then incubated with antibodies specific to acid alpha-glucosidase (GAA, the protein of interest) and b-actin (used as an internal quality control protein). A chemiluminescent substrate is added to the membrane and the emitted light signal is captured by digital imaging. If specific bands are present, the patient is determined to be cross-reactive immunologic material (CRIM)-positive while the absence of these bands indicates a CRIM-negative result.(Wang Z, Okamoto P, Keutzer J: A new assay for fast, reliable CRIM status determination in infantile-onset Pompe disease. Mol Genet Metab. 2014;111:92-100)

PDF Report

No

Specimen Retention Time

3 years-Check with the lab for availability

Performing Laboratory Location

Rochester

Fees & Codes

Test Classification

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

CPT Code Information

84182-Pompe CRIM
88233-Fibroblast culture
88240-Cryopreservation for biochemical studies