

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

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.

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](#)

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

[Biochemical Genetics Patient Information](#) (T602) in Special Instructions.

Reject Due To

| | |
|---|----------|
| Specimen in formalin or fixative preservative | Â Reject |
|---|----------|

Specimen Stability Information

| Specimen Type | Temperature | Time | Special Container |
|---------------|-------------|------|-------------------|
| Tissue | Varies | | |

Clinical and 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.

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, DeArme 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 D, Beaudet AL, Vogelstein B, et al, eds. *The Online Metabolic and Molecular Bases of Inherited Disease*. McGraw-Hill, 2014. Accessed May 10, 2019. Available at <https://ommbid.mhmedical.com/content.aspx?sectionid=225890450&bookid=2709&Resultclick=2>

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

Day(s) Performed

Varies

Report Available

30 to 45 days

Specimen Retention Time

3 years-Check with the lab for availability

Performing Laboratory Location

Rochester

Fees and 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 Regional Manager. 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. This test has not been cleared or approved by the U.S. Food and Drug Administration.

CPT Code Information

84182-Pompe CRIM

88233-Fibroblast culture

88240-Cryopreservation for biochemical studies

LOINC® Information

| Test ID | Test Order Name | Order LOINC Value |
|---------|----------------------------------|-------------------|
| PDCRF | Pompe Disease CRIM Status, Fibro | In Process |

| Result ID | Test Result Name | Result LOINC Value |
|-----------|------------------|--------------------|
| 606123 | GAA CRIM status | In Process |
| 606124 | Interpretation | 59462-2 |
| 606125 | Reviewed By | 18771-6 |

