Test Definition: PDCRW

Pompe Disease CRIM Status, WBC

Overview

Useful For

Determination of cross-reactive immunologic material status using leukocytes from 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.

Testing Algorithm

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

Western Blot

NY State Available

Yes

Specimen

Specimen Type

Whole blood

Shipping Instructions

For optimal isolation of leukocytes, it is recommended the specimen arrive refrigerated within 7 days of collection to be stabilized. Collect specimen Monday through Thursday only and not the day before a holiday. Specimen should be collected and packaged as close to shipping time as possible.

Specimen Required

Supplies: Vacutainer 4.0 mL CPT Mononuclear Cell Preparation Tube (T840)

Specimen Volume: 4 mL

Collection Instructions:

1. Collect 4 mL blood in CPT mononuclear cell preparation tube.

2. Mix by inversion 6 to 8 times.

3. Centrifuge at 1800xg for 30 minutes within 2 hours of collection.

4. Send CPT tube on cold packs. **Do not aliquot plasma.**

Forms

Biochemical Genetics Patient Information (T602) in Special Instructions.

Specimen Minimum Volume

2 mL

Reject Due To

Gross hemolysis	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Whole blood	Refrigerated	7 days	NaCit BLUBLK CellPrep

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 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 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 peripheral blood mononuclear cells (PBMC). 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

2 months

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

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
PDCRW	Pompe Disease CRIM Status, WBC	In Process

Result ID	Test Result Name	Result LOINC Value
606127	GAA CRIM status	In Process
606128	Interpretation	59462-2
606129	Reviewed By	18771-6