Test Definition: GALE

Uridine Diphosphate-Galactose 4' Epimerase, Blood

Overview

Useful For
Diagnosis of uridine diphosphate-galactose 4' epimerase deficiency

Genetics Test Information
Enzymatic testing for the diagnosis of uridine diphosphate-galactose 4' epimerase deficiency.

Testing Algorithm
For more information see Galactosemia Testing Algorithm.

Special Instructions
- Informed Consent for Genetic Testing
- Galactosemia Testing Algorithm
- Biochemical Genetics Patient Information
- Informed Consent for Genetic Testing (Spanish)
- Galactosemia-Related Test List

Method Name
Enzyme Reaction followed by Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS)

NY State Available
Yes

Specimen

Specimen Type
Whole Blood EDTA

Ordering Guidance
This test is appropriate for diagnosis of uridine diphosphate-galactose 4' epimerase (GALE) deficiency, but it will **not** detect galactokinase (GALK) deficiency, galactose-1-phosphate uridyltransferase (GALT) deficiency, or galactose mutarotase (GALM) deficiency.
-To evaluate for GALK deficiency, order GALK / Galactokinase, Blood.
-To evaluate for GALT deficiency, order GALT / Galactose-1-Phosphate Uridyltransferase, Blood.
-To evaluate for GALM deficiency, order GALP / Galactose, Plasma and molecular analysis of the *GALM* gene.

This assay is **not appropriate** for monitoring dietary compliance for patients with GALE deficiency. If dietary monitoring is needed, order GAL1P / Galactose-1-Phosphate, Erythrocytes.

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Necessary Information

Patient's age is required.

Biochemical Genetics Patient Information (T602) is recommended, but not required, to be filled out and sent with the specimen to aid in the interpretation of test results.

Specimen Required

Multiple whole blood tests for galactosemia can be performed on 1 specimen. Prioritize order of testing when submitting specimens. For a list of tests that can be ordered together, see Galactosemia-Related Test List.

Container/Tube:
Preferred: Lavender top (EDTA)
Acceptable: Green top (sodium or lithium heparin) or yellow top (ACD)
Specimen Volume: 5 mL

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:
-Informed Consent for Genetic Testing (T576)
-Informed Consent for Genetic Testing-Spanish (T826)
2. Biochemical Genetics Patient Information (T602) is recommended.
3. If not ordering electronically, complete, print, and send a Biochemical Genetics Test Request (T798) with the specimen.

Specimen Minimum Volume

2 mL

Reject Due To

Gross hemolysis	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Whole Blood EDTA	Refrigerated (preferred)	14 days	
	Ambient	6 days	

Clinical & Interpretive

Clinical Information

Galactosemia is an autosomal recessive disorder that results from a deficiency of any 1 of the 4 enzymes catalyzing the conversion of galactose to glucose: galactose-1-phosphate uridyltransferase (GALT), galactokinase (GALK), uridine

diphosphate galactose-4-epimerase (GALE), and galactose mutarotase (GALM).

Epimerase deficiency galactosemia can be categorized into 3 types: generalized, peripheral, and intermediate. Generalized epimerase deficiency galactosemia is rare with less than 10 cases described in the literature and results in profoundly decreased enzyme activity in all tissues, whereas peripheral epimerase deficiency galactosemia results in decreased enzyme activity in red and white blood cells, but normal enzyme activity in all other tissues. This is compared to intermediate epimerase deficiency galactosemia, which results in decreased enzyme activity in red and white blood cells and less than 50% of normal enzyme levels in other tissues.

Clinically, infants with generalized epimerase deficiency galactosemia develop symptoms such as liver and kidney dysfunction and mild cataracts when on a normal milk diet, while infants with peripheral or intermediate epimerase deficiency galactosemia do not develop any symptoms. Generalized epimerase deficiency galactosemia is treated by a galactose- and lactose-restricted diet, which can improve or prevent the symptoms of kidney and liver dysfunction and mild cataracts. Despite adequate treatment from an early age, individuals with generalized epimerase deficiency galactosemia remain at increased risk for developmental delay and intellectual disability. Unlike patients with classic galactosemia resulting from a GALT deficiency, female patients with generalized epimerase deficiency galactosemia experience normal puberty and are not at increased risk for premature ovarian failure. Based upon reports by newborn screening programs, the frequency of epimerase deficiency galactosemia in the United States ranges from approximately 1 in 6700 African American infants to 1 in 70,000 infants of European ancestry.

Galactose-1-phosphate (Gal1P) accumulates in the erythrocytes of patients with galactosemia due to either GALT or GALE deficiency or in neonates with GALM deficiency. The quantitative measurement of Gal1P (GAL1P / Galactose-1-Phosphate, Erythrocytes) is useful for monitoring compliance with dietary therapy. Gal1P is thought to be the causative factor for development of liver disease in patients with GALT or GALE deficiency. Because of this, patients should maintain low levels and be monitored on a regular basis.

Newborn screening varies from state to state and identifies potentially affected individuals by measuring total galactose (galactose and Gal1P) or determining the activity of the GALT enzyme. The diagnosis of galactosemia is established by follow-up quantitative measurement of GALT enzyme activity. If enzyme levels are normal, but an infant has an elevated Gal-1-P, then epimerase deficiency galactosemia should be considered. Molecular analysis of the *GALE* gene is available; order CGPH / Custom Gene Panel, Hereditary, Next-Generation Sequencing, Varies and specify Gene List ID: IEMCP-MGXGL2.

For more information see Galactosemia Testing Algorithm.

Reference Values

> or =3.5 nmol/h/mg of hemoglobin

Interpretation

Results below 3.5 nmol/h/mg of hemoglobin in properly submitted specimens have different causes from carrier status for a disease-causing variant in the *GALE* gene (typically reduced uridine diphosphate-galactose 4' epimerase [GALE] activity close to the normal activity range) to generalized epimerase deficiency galactosemia due to biallelic disease-causing variants in the *GALE* gene that markedly reduce GALE activity. Further differentiation requires additional biochemical and molecular genetic analyses as well as correlation with clinical signs and symptoms.

Normal results (> or =3.5 nmol/hour/mg of hemoglobin) are not consistent with galactosemia due to GALE deficiency.

Cautions

The results of testing performed in erythrocytes, including analysis of enzymes, biochemical phenotyping, or galactose-1-phosphate are invalid following a transfusion.

Clinical Reference

1. Fridovich-Keil J, Bean L, He M, Schroer R. Epimerase deficiency galactosemia. In: Adam MP, Feldman J, Mirzaa GM,, et al. eds. GeneReviews [Internet]. University of Washington, Seattle; 2011. Updated March 11, 2021. Accessed September 12, 2024. Available at www.ncbi.nlm.nih.gov/books/NBK51671/

2. Walter JH, Fridovich-Keil JL. Galactosemia. In: Valle D, Antonarakis S, Ballabio A, Beaudet AL, Mitchell GA, eds. The Online Metabolic and Molecular Bases of Inherited Disease. McGraw-Hill; 2019. Accessed September 12, 2024. Available at https://ommbid.mhmedical.com/content.aspx?bookid=2709&sectionid=%20225081023

3. Timson DJ. Type IV galactosemia. Genet Med. 2019;21(6):1283-1285. doi:10.1038/s41436-018-0359-z

4. Wada Y, Kikuchi A, Arai-Ichinoi N, et al. Biallelic GALM pathogenic variants cause a novel type of galactosemia. Genet Med. 2019;21(6):1286-1294. doi:10.1038/s41436-018-0340-x

Performance

Method Description

A buffered enzyme incubation with substrate and cofactors is performed on lysed red blood cells. A post-incubation extraction is performed and subjected to liquid chromatography-tandem mass spectrometry. The ratio of the extracted product to its internal standard is used to calculate the total enzymatic product. This is then normalized using the calculated hemoglobin concentration to determine the patient's enzyme level in nmol/h/mg of hemoglobin.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Friday

Report Available

6 to 12 days

Specimen Retention Time

2 months

Performing Laboratory Location

Mayo Clinic Laboratories - Rochester Main Campus

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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

82542

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
GALE	UDP-galactose 4' epimerase, RBC	79469-3

Result ID	Test Result Name	Result LOINC® Value
64372	UDP-galactose 4' epimerase, RBC	79469-3
37979	Interpretation (GALE)	59462-2
37978	Reviewed By	18771-6