Test Definition: GALTZ

GALT Gene, Full Gene Analysis

Overview

Useful For

Identifying mutations in individuals who test negative for the common mutations and who have a biochemical diagnosis of galactosemia or galactose-1-phosphate uridyltransferase activity levels indicative of carrier status

Genetics Test Information

Not the preferred first-tier molecular test for carrier screening or diagnosis. Used to identify mutations in individuals with a clinical diagnosis of galactosemia when GAL14 / Galactosemia Gene Analysis (14-Mutation Panel) is negative or uninformative.

Testing Algorithm

See Galactosemia Testing Algorithm in Special Instructions.

Special Instructions

- Molecular Genetics: Congenital Inherited Diseases Patient Information
- Informed Consent for Genetic Testing
- Galactosemia Testing Algorithm
- Blood Spot Collection Card-Spanish Instructions
- Blood Spot Collection Card-Chinese Instructions
- Informed Consent for Genetic Testing (Spanish)
- Galactosemia-Related Test List
- Blood Spot Collection Instructions

Method Name

Polymerase Chain Reaction (PCR) Amplification/DNA Sequencing

NY State Available

Yes

Specimen

Specimen Type

Varies

Shipping Instructions

Specimen preferred to arrive within 96 hours of draw.

Specimen Required

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

Patient Preparation: A previous bone marrow transplant from an allogenic donor will interfere with testing. Call 800-533-1710 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 specimen in original tube.

Specimen Stability Information: Ambient (preferred)/Refrigerated

Specimen Type: Blood spot

Supplies: Card - Blood Spot Collection (Filter Paper) (T493)

Container/Tube:

Preferred: Collection card (Whatman Protein Saver 903 Paper)

Acceptable: Ahlstrom 226 filter paper, or Blood Spot Collection Card

Specimen Volume:2 to 5 Blood Spots on collection card (Whatman Protein Saver 903 Paper; Ahlstrom 226 filter paper; or Blood Spot Collection Card)

Collection Instructions:

1. An alternative blood collection option for a patient >1 year of age is finger stick.

2. Let blood dry on the filter paper at ambient temperature in a horizontal position for 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. For collection instructions, see Blood Spot Collection Instructions in Special Instructions.

2. For collection instructions in Spanish, see Blood Spot Collection Card-Spanish Instructions (T777) in Special Instructions.

3. For collection instructions in Chinese, see Blood Spot Collection Card-Chinese Instructions (T800) in Special Instructions.

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 an Inborn Errors of Metabolism 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 by Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Ambient (preferred)		
	Frozen		
	Refrigerated		

Clinical and Interpretive

Clinical Information

Classic galactosemia is an autosomal recessive disorder of galactose metabolism caused by mutations in the galactose-1-phosphate uridyltransferase (*GALT*) gene. The complete or near complete deficiency of the GALT enzyme is life threatening. If left untreated, complications include liver failure, sepsis, mental retardation, and death. Galactosemia is treated by a galactose-free diet, which allows for rapid recovery from the acute symptoms and a generally good prognosis. Despite adequate treatment from an early age, children with galactosemia remain at increased risk for developmental delays, speech problems, and abnormalities of motor function. Females with galactosemia are at increased risk for premature ovarian failure. The prevalence of classic galactosemia is approximately 1 in 30,000.

Duarte variant galactosemia (compound heterozygosity for the Duarte variant, N314D, and a classic mutation) is generally associated with higher levels of GALT activity (5%-20%) than classic galactosemia (<5%); however, this may be indistinguishable by newborn screening assays. Typically, individuals with Duarte variant galactosemia have

a milder phenotype, but are often treated with a low galactose diet during infancy. The LA variant, consisting of N314D and a second change, L218L, is associated with higher levels of GALT activity than the Duarte variant alone.

Newborn screening, which identifies potentially affected individuals by measuring total galactose (galactose and galactose-1-phosphate) and/or determining the activity of the GALT enzyme, varies from state to state. The diagnosis of galactosemia is established by follow-up quantitative measurement of GALT activity. If enzyme activity levels are indicative of carrier or affected status, molecular testing for common *GALT* mutations may be performed. If 1 or both disease-causing mutations are not detected by targeted mutation analysis and biochemical testing has confirmed the diagnosis of galactosemia, sequencing of the *GALT* gene is available to identify private mutation(s).

The *GALT* gene maps to 9p13. More than 180 mutations have been identified in the *GALT* gene. Several disease-causing mutations are common in patients with classic galactosemia (G/G genotype). The most frequently observed is the Q188R mutation. This mutation accounts for 60% to 70% of classic galactosemia alleles. The S135L mutation is the most frequently observed mutation in African Americans and accounts for approximately 50% of the mutant alleles in this population. The K285N mutation is common in those of eastern European descent and accounts for 25% to 40% of the alleles in this population. The L195P mutation is observed in 5% to 7% of classic galactosemia. The Duarte variant (N314D) is found in 5% of the general United States population.

The above mutations, plus the LA variant, are included in GCT / Galactosemia Reflex, Blood, which is the preferred test for the diagnosis of galactosemia or for follow-up to positive newborn screening results. These mutations are also included in GAL14 / Galactosemia Gene Analysis (14-Mutation Panel). Full sequencing of the *GALT* gene can be useful for the identification of mutations when 1 or no mutations are found with these tests in an individual with demonstrated GALT activity deficiency. Full sequencing of the *GALT* gene identifies over 95% of the sequence variants in the coding region and splice junctions. See Galactosemia Testing Algorithm in Special Instructions for additional information.

Reference Values

An interpretive report will be provided.

Interpretation

All detected alterations will be evaluated according to the American College of Medical Genetics and Genomics (AMCG) recommendations.(1) Variants will be 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 galactosemia may have a mutation that is not identified by the methods described above (eg, large genomic deletions, promoter mutations). The absence of a mutation(s), therefore, does not eliminate the possibility of positive carrier status or the diagnosis of galactosemia. For carrier testing, it is important to first document the presence of a galactose-1-phosphate uridyltransferase (*GALT*) gene mutation in an affected family member.

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

Rare polymorphisms exist that could lead to false-negative or false-positive results. If results obtained do not match the clinical and biochemical 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 our interpretation of results may occur if information given is inaccurate or incomplete.

This test is **not** recommended for carrier screening or diagnosis in individuals with a positive newborn screen; see GCT / Galactosemia Reflex, Blood.

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. Elsas LJ 2nd, Lai K: The molecular biology of galactosemia. Genet Med 1998 Nov-Dec;1(1):40-48

3. Novelli G, Reichardt JK: Molecular basis of disorders of human galactose metabolism: past, present, and future. Mol Genet Metab 2000 Sep-Oct;71(1-2):62-65

4. Bosch AM, Ijlst L, Oostheim W, et al: Identification of novel mutations in classical galactosemia. Hum Mutat 2005 May;25(5):502

Performance

Method Description

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

PDF Report

No

Day(s) and Time(s) Test Performed

Performed weekly, varies

Analytic Time

14 days

Maximum Laboratory Time

20 days

Specimen Retention Time

Whole Blood: 2 weeks (if available) Extracted DNA: 3 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

81406-GALT (galactose-I-phosphate uridylyltransferase) (eg, galactosemia), full gene sequence

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
GALTZ	GALT Gene, Full Gene Analysis	76037-1

Result ID	Test Result Name	Result LOINC Value
53922	Result Summary	50397-9
53923	Result	82939-0
53924	Interpretation	69047-9
53925	Additional Information	48767-8
53926	Specimen	31208-2
53927	Source	31208-2
53928	Released By	18771-6