

Overview

Useful For

Diagnosis of Krabbe disease

Follow-up testing for evaluation of an abnormal newborn screening result for Krabbe disease

This test is **not intended for** carrier detection.

Genetics Test Information

This test provides diagnostic testing for patients with clinical signs and symptoms suspicious for Krabbe disease.

Enzyme testing for galactocerebrosidase is included in the diagnostic workup for infants following a positive newborn screen result for Krabbe disease.

Testing Algorithm

The following information is available:

[-Newborn Screen Follow-up for Krabbe Disease: Galactocerebrosidase](#)

[-Newborn Screen Follow-up for Krabbe Disease: Galactocerebrosidase and Psychosine](#)

[-Newborn Screen Follow-up for Krabbe Disease: Galactocerebrosidase, Psychosine, and GALC 30kb Deletion](#)

[-Newborn Screening Act Sheet Krabbe Disease: Decreased Galactocerebrosidase](#)

Special Instructions

- [Informed Consent for Genetic Testing](#)
- [Biochemical Genetics Patient Information](#)
- [Newborn Screening Act Sheet Krabbe Disease: Decreased Galactocerebrosidase](#)
- [Informed Consent for Genetic Testing \(Spanish\)](#)
- [Newborn Screen Follow-up for Krabbe Disease: Galactocerebrosidase](#)
- [Newborn Screen Follow-up for Krabbe Disease: Galactocerebrosidase and Psychosine](#)
- [Newborn Screen Follow-up for Krabbe Disease: Galactocerebrosidase, Psychosine, and GALC 30kb Deletion](#)

Method Name

Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS)

NY State Available

Yes

Specimen**Specimen Type**

Whole Blood ACD

Ordering Guidance

This test will not detect carrier status. For differentiating alterations from disease-causing variants in affected patients and for carrier detection in family members, molecular sequencing of the *GALC* gene is necessary. Order KRABZ / Krabbe Disease, Full Gene Analysis and Large (30 kb) Deletion, Varies.

Shipping Instructions

For optimal isolation of leukocytes, it is recommended the specimen arrive refrigerate within 6 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**Container/Tube:**

Preferred: Yellow top (ACD solution B)

Acceptable: Yellow top (ACD solution A) or lavender top (EDTA)

Specimen Volume: 6 mL

Collection Instructions: Send whole blood specimen in original tube. **Do not aliquot.**

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 \(T602\)](#)

3. If not ordering electronically, complete, print, and send a [Biochemical Genetics Test Request \(T798\)](#) with the specimen.

Reject Due To

Gross hemolysis Reject

Specimen Minimum Volume

2 mL

Specimen Stability Information

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

Clinical & Interpretive**Clinical Information**

Krabbe disease (globoid cell leukodystrophy) is an autosomal recessive disorder caused by a deficiency of the enzyme, galactocerebrosidase (GALC). GALC facilitates the lysosomal degradation of psychosine (galactosylsphingosine) and 3 other substrates (galactosylceramide, lactosylceramide, and lactosylsphingosine causing severe demyelination throughout the brain. Krabbe disease is caused by variants in the *GALC* gene, and it has an estimated frequency of 1 in 100,000 births. Although rare, a few infants with an infantile Krabbe disease-like phenotype due to deficiency of saposin A have been found. Saposin-A is a sphingolipid activator protein that assists galactocerebrosidase in its action on galactosylceramide.

Severely affected infants typically present between 3 to 6 months of age with increasing irritability and sensitivity to stimuli. Rapid neurodegeneration including white matter disease follows, with death usually occurring by age 2 years. Some individuals have later onset forms of the disease that are characterized by ataxia, vision loss, weakness, and psychomotor regression presenting anywhere from age 6 months to the seventh decade of life. The clinical course of Krabbe disease can be variable, even within the same family.

Newborn screening for Krabbe disease has been implemented in some states. The early (presymptomatic) identification and subsequent testing of infants at risk for Krabbe disease may be helpful in reducing the morbidity and mortality associated with this disease. While treatment is mostly supportive, hematopoietic stem cell transplantation has shown some success if performed early, prior to onset of neurologic damage.

Reduced or absent galactocerebrosidase in leukocytes can indicate a diagnosis of Krabbe disease; however, a number of alterations in the *GALC* gene have been identified that result in reduced galactocerebrosidase activity in vitro but do not

cause disease. The biomarker, psychosine (PSY / Psychosine, Blood Spot or PSYR / Psychosine, Whole Blood or PSYCF / Psychosine, Spinal Fluid), has been shown to be elevated in patients with active Krabbe disease. Molecular sequencing of the *GALC* gene (KRABZ / Krabbe Disease, Full Gene Analysis and Large [30 kb] Deletion, Varies) is necessary for differentiating alterations from disease-causing variants in affected patients and for carrier detection in family members.

Reference Values

> or =0.300 nmol/hour/mg protein

An interpretative report will be provided.

Interpretation

When abnormal results are detected, a detailed interpretation is given, including an overview of the results and of their significance, a correlation to available clinical information, elements of differential diagnosis, recommendations for additional biochemical testing, and in vitro, confirmatory studies (enzyme assay, molecular analysis), name and phone number of key contacts who may provide these studies, and a phone number to reach one of the laboratory directors in case the referring physician has additional questions.

Cautions

Pseudodeficiency of galactocerebrosidase causes reduced enzymatic activity but does not cause disease.

A Krabbe disease phenotype can also be caused in very rare cases by the absence of a physiologically active sphingolipid activator protein, saposin A.

Enzyme levels may be normal in individuals who have undergone hematopoietic stem cell transplant.

Clinical Reference

1. Elliott S, Buroker N, Cournoyer JJ, et al: Pilot study of newborn screening for six lysosomal storage diseases using Tandem Mass Spectrometry. *Mol Genet Metab.* 2016 Aug;118(4):304-309
2. Matern D, Gavrilov D, Oglesbee D, Raymond K, Rinaldo P, Tortorelli S: Newborn screening for lysosomal storage disorders. *Semin Perinatol.* 2015 Apr;39(3):206-216
3. Orsini JJ, Escolar ML, Wasserstein MP, et al: Krabbe disease. In: Adam MP, Ardinger HH, Pagon RA, et al, eds. *GeneReviews* [Internet]. University of Washington, Seattle; 2000. Updated October 11, 2018. Accessed April 5, 2022. Available at www.ncbi.nlm.nih.gov/books/NBK1238/
4. Liao HC, Spacil Z, Ghomashchi F, et al: Lymphocyte galactocerebrosidase activity by LC-MS/MS for post-newborn screening evaluation of Krabbe disease. *Clin Chem.* 2017 Aug;63(8):1363-1369
5. Kwon JM, Matern DM, Kurtzberg J, et al: Consensus guidelines for newborn screening, diagnosis and treatment of

infantile Krabbe disease. Orphanet J Rare Dis. 2018;13:30 doi: 10.1186/s13023-018-0766-x

Performance

Method Description

The specimens are incubated with a mix of substrate and internal standard for galactocerebrosidase and alpha galactosidase (GLA). The reaction is then stopped using acetonitrile, centrifuged, and a portion of the supernatant is prepared for analysis by liquid chromatography-tandem mass spectrometry. GLA is included to verify sample integrity.(Unpublished Mayo method)

PDF Report

No

Specimen Retention Time

WBC homogenate: 1 month

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

82657

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
GALCW	Galactocerebrosidase, WBC	24084-6

Result ID	Reporting Name	LOINC®
606270	Galactocerebrosidase, WBC	24084-6
606271	Interpretation	59462-2

606272	Reviewed By	18771-6
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