Overview

Useful For

Aids in the biochemical diagnosis of Krabbe disease and saposin A cofactor deficiency

Follow-up of individuals affected with Krabbe disease

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

This test is **not** capable of identifying carriers of Krabbe disease.

Genetics Test Information

Krabbe disease (globoid cell leukodystrophy) is an autosomal recessive lysosomal storage disorder caused by an enzyme deficiency of galactocerebrosidase (GALC).

Although Krabbe disease is clinically variable, the most common and severe form of the disorder is early infantile onset that presents with rapid neurological regression and results in early death.

This test is a second-tier assay for infants who have abnormal newborn screens with reduced GALC activity and can diagnose patients with Krabbe disease or saposin A cofactor deficiency.

Testing Algorithm

The following are 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

- Biochemical Genetics Patient Information
- Blood Spot Collection Card-Spanish Instructions
- Newborn Screening Act Sheet Krabbe Disease: Decreased Galactocerebrosidase
- Blood Spot Collection Card-Chinese Instructions
- 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
- Blood Spot Collection Instructions

Highlights

Elevations in psychosine support a diagnosis of Krabbe disease; therefore, psychosine quantitation is a useful biomarker in determining if an individual has active disease and can aid in monitoring disease progression or treatment response.

Psychosine is also elevated in saposin A cofactor deficiency, which results in a similar clinical phenotype to Krabbe disease, but patients have normal galactocerebrosidase (GALC) activity.

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

NY State Available
Yes

Specimen

Specimen Type
Whole blood

Ordering Guidance
This test is recommended for newborns or infants who have not had previous psychosine testing.

If requesting psychosine testing for either diagnostic or monitoring purposes, order PSYR / Psychosine, Whole Blood.

Specimen Required
Supplies: Card-Blood Spot Collection (Filter Paper) (T493)
Container/Tube:
Preferred: Card-Blood Spot Collection (Filter Paper)
Acceptable: PerkinElmer 226 (formerly Ahlstrom 226) filter paper, Munktell filter paper, Whatman protein Saver 903 paper, or blood collected in tubes containing EDTA (preferred) or heparin and dried on filter paper
Specimen Volume: 2 blood spots
Collection Instructions:
1. Completely fill at least 2 circles on the filter paper card (approximately 100 microliters blood per circle).
2. Let blood dry on filter paper at ambient temperature in a horizontal position for a minimum of 3 hours.
3. Do not expose specimen to heat or direct sunlight.
4. Do not stack wet specimens.
5. Keep specimen dry.
Additional Information:
1. For collection instructions, see Blood Spot Collection Instructions
2. For collection instructions in Spanish, see Blood Spot Collection Card-Spanish Instructions (T777)
3. For collection instructions in Chinese, see Blood Spot Collection Card-Chinese Instructions (T800)

Forms
1. Biochemical Genetics Patient Information (T602)
2. If not ordering electronically, complete, print, and send an Inborn Errors of Metabolism Test Request (T798) with the specimen.

Specimen Minimum Volume
1 Blood spot

Reject Due To

Blood spot showing serum rings Insufficient specimen Layering Multiple applications Nonapproved filter paper	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Whole blood	Ambient (preferred)	96 days	FILTER PAPER
	Frozen	96 days	FILTER PAPER
	Refrigerated	96 days	FILTER PAPER

Clinical & Interpretive

Clinical Information

Krabbe disease (globoid cell leukodystrophy) is an autosomal recessive lysosomal storage disorder caused by an enzyme deficiency of galactocerebrosidase (GALC). GALC facilitates the lysosomal degradation of psychosine (galactosylsphingosine) and 3 other substrates, galactosylceramide, lactosylceramide, and lactosylsphingosine. Krabbe disease is caused by variants in the *GALC* gene, and it has an estimated frequency of 1 in 100,000 births.

Eighty-five percent to 90% of patients present before the first year of life with central nervous system impairment including increasing irritability, developmental delay, and sensitivity to stimuli. Rapid neurodegeneration including white matter disease follows, with death usually occurring by 2 years of age. Ten percent to 15% of individuals have late onset forms of the disease that are characterized by ataxia, vision loss, weakness, and psychomotor regression presenting anytime 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, usually within the first 2 months of life.

Psychosine is 1 of 4 substrates degraded by GALC and is a neurotoxin at elevated concentrations. It has been shown to be elevated in patients with active Krabbe disease or with saposin A cofactor deficiency and, therefore, may be a useful biomarker for the presence of disease or disease progression.

Reduced or absent GALC in leukocytes (GALCW / Galactocerebrosidase, Leukocytes) or dried blood spots (PLSD / Lysosomal and Peroxisomal Storage Disorders Screen, Blood Spot) along with psychosine analysis can indicate a diagnosis of Krabbe disease. Molecular sequencing of the *GALC* gene (KRABZ / Krabbe Disease, Full Gene Analysis and Large [30 kb] Deletion, Varies) allows for detection of the disease-causing variants in affected patients and carrier detection in family members.

Individuals with a disease phenotype similar to Krabbe disease may have saposin A cofactor deficiency. Saposin A cofactor deficiency also results in elevated psychosine levels. Testing for this condition via molecular analysis of the *PSAP* gene is useful in those with elevated psychosine and normal to reduced GALC activity with normal molecular genetic *GALC* sequencing.

Reference Values

Normal <2 nmol/L psychosine

Interpretation

An interpretive report will be provided.

An elevation of psychosine is indicative of symptomatic Krabbe disease or symptomatic saposin A cofactor deficiency.

Cautions

Psychosine levels may be normal in patients who are not yet symptomatic or have later onset Krabbe disease or saposin A cofactor deficiency.

Supportive Data

Receiver operating characteristic curve analysis of 220 controls and 6 patients affected with Krabbe disease yielded an area under the curve of 1.0, permitting the selection of a cutoff value yielding a positive predictive value and negative predictive value of 1.0.

Clinical Reference

1. Orsini JJ, Morrissey MA, Slavin LN, et al: Implementation of newborn screening for Krabbe disease: population study and cutoff determination. Clin Biochem. 2009 Jun;42(9):877-884. doi: 10.1016/j.clinbiochem.2009.01.022
2. Svennerholm L, Vanier MT, Mansson JE: Krabbe disease: a galactosylsphingosine (psychosine) lipidosis. J Lipid Res. 1980 Jan;21(1):53-64
3. Enns GM, Steiner RD, Cowan TM: Lysosomal disorders. In: Sarafoglou K, Hoffman G, Roth KS, eds. Pediatric Endocrinology and Inborn Errors of Metabolism. McGraw-Hill Medical; 2009:744
4. Turgeon CT, Orsini JJ, Sanders KA, et al: Measurement of psychosine in dried blood spots--a possible improvement to newborn screening programs for Krabbe disease. J Inherit Metab Dis. 2015 Sep;38(5):923-929. doi: 10.1007/s10545-015-9822-z
5. Wenger DA, Escolar ML, Luzi P, Rafi MA: Krabbe disease (globoid cell leukodystrophy). 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 November 16, 2021. Available at https://ommbid.mhmedical.com/content.aspx?sectionid=225546481&bookid=2709
6. Guenzel AJ, Turgeon CT, Nickander KK, et al: The critical role of psychosine in screening, diagnosis, and monitoring of Krabbe disease. Genet Med. 2020 Jun;22(6):1108-1118. doi: 10.1038/s41436-020-0764-y
7. Thompson-Stone R, Ream MA, Gelb M, et al: Consensus recommendations for the classification and long-term follow up of infants who screen positive for Krabbe disease. Mol Genet Metab. 2021 Sep-Oct;134(1-2):53-59. doi: 10.1016/j.ymgme.2021.03.016

Performance

Method Description

Internal standard is added to a dried blood spot. The extract is evaporated and reconstituted prior to injection onto a liquid chromatography-tandem mass spectrometry (LC-MS/MS). Following separation of the structural isomers glucopsychosine and psychosine (PSY) by liquid chromatography, their concentrations are measured by MS/MS analysis in the multiple reaction monitoring positive mode to follow the precursor to product species transitions for PSY. The ratio of the extracted peak area of PSY to internal standard as determined by LC-MS/MS is used to calculate the concentration of PSY in the sample.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Monday through Sunday

Report Available

1 to 2 days

Specimen Retention Time

1 year

Performing Laboratory Location

Rochester

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 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 US Food and Drug Administration.

CPT Code Information

82542

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
PSY	Psychosine, BS	93688-0

Result ID	Test Result Name	Result LOINC® Value
62235	Psychosine	93688-0
36342	Reviewed By	18771-6

36343	Interpretation (PSY)	59462-2