Test Definition: NCLBS

Neuronal Ceroid Lipofuscinosis, Two-Enzyme Panel, Blood Spot

Overview

Useful For

Supporting the biochemical diagnosis of two neuronal ceroid lipofuscinoses, CLN1 and CLN2

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

Genetics Test Information

This test provides diagnostic testing for individuals with clinical signs and symptoms suspicious for neuronal ceroid lipofuscinosis 1 or 2 (CLN1 or CLN2). If an enzyme deficiency is detected by this screening test, additional biochemical or molecular testing is required to confirm a diagnosis.

Special Instructions

- Informed Consent for Genetic Testing
- Biochemical Genetics Patient Information
- Blood Spot Collection Card-Spanish Instructions
- Blood Spot Collection Card-Chinese Instructions
- Blood Spot Collection Instructions

Method Name

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

NY State Available

Yes

Specimen

Specimen Type

Whole blood

Ordering Guidance

This blood test is an appropriate first step for individuals between 0 and 4 years of age who present with symptoms consistent with neuronal ceroid lipofuscinosis.

Necessary Information

1. Patient's age is required.

2. Reason for testing is required

Specimen Required

Submit only 1 of the following specimen types:

Preferred:
Specimen Type: Blood spot
Supplies: Card-Blood Spot Collection (Filter Paper) (T493)
Container/Tube:
Preferred: Blood Spot Collection Card
Acceptable: Whatman Protein Saver 903 Paper, PerkinElmer 226 filter paper, Munktell filter paper, or blood collected in tubes containing ACD or EDTA and dried on filter paper.
Specimen Volume: 2 Blood spots
Collection Instructions:
1. An alternative blood collection option for a patient older than 1 year is a fingerstick. For detailed instructions, see How to Collect a Dried Blood Spot Sample.
2. At least 2 spots should be complete, ie, unpunched.
3. Let blood dry on filter paper at room temperature in a horizontal position for a minimum of 3 hours.
4. Do not expose specimen to heat or direct sunlight.
5. Do not stack wet specimens.
6. Keep specimen dry.
Specimen Stability Information: Refrigerated (preferred) 60 days/Ambient 7 days/Frozen 60 days
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).

Acceptable:
Specimen Type: Whole Blood
Container/Tube:
Preferred: Lavender top (EDTA)
Acceptable: Yellow top (ACD)
Specimen Volume: 2 mL
Collection Instructions: Send whole blood specimen in original tube**. Do not aliquot.**
Specimen Stability Information: Refrigerate (preferred) 7 days/Ambient 48 hours

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.

Specimen Minimum Volume

Blood Spots: 1; Whole Blood: 0.5 mL

Reject Due To

Blood spot specimen that shows serum rings or has multiple layers	Reject
Insufficient specimen	Reject
Unapproved filter papers	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Whole blood	Varies		

Clinical & Interpretive

Clinical Information

The neuronal ceroid lipofuscinoses (NCL) comprise a group of recessively inherited neurodegenerative disorders involved in lysosomal protein catabolism. Clinically they are characterized by vision loss, seizures, developmental regression, behavioral changes, movement disorders, and distinguished from other neurodegenerative disorders by the accumulation of auto fluorescent storage material in the brain and tissues. Although at least 13 different genes have been identified, NCL have traditionally been categorized based on the age of onset of symptoms: infantile, late-infantile, juvenile, and adult. Infantile NCL (CLN1) and late-infantile NCL (CLN2) are caused by defects in palmitoyl-protein thioesterase 1 (*PPT1)* and tripeptidyl peptidase 1 (*TPP1)*, respectively. Deficiency of tripeptidyl peptidase is also a cause of autosomal recessive spinocerebellar ataxia-7.

Children affected by infantile NCL (CLN1) typically have normal growth and development until about 6 to 12 months of age. Slowed head growth occurs at around 9 months followed by psychomotor degeneration, seizures, and progressive macular degeneration leading to blindness by the age 2 years. CLN1 is caused by a deficiency of the lysosomal enzyme palmitoyl-protein thioesterase 1 (PPT1), which cleaves long-chain fatty acids (usually palmitate) from cysteine residues. Electron microscopy shows granular osmophilic deposits in most cell types. PPT1 is thought to play an active role in various cell processes including apoptosis, endocytosis, and lipid metabolism.

The late infantile form of NCL (CLN2) is primarily caused by deficiency of the lysosomal enzyme tripeptidyl peptidase 1 (TPP1), which cleaves tripeptides from the N-terminus of polypeptides. Tissue damage results from the defective degradation and consequent accumulation of storage material with a curvilinear profile by electron microscopy. There is widespread loss of neuronal tissue especially in the cerebellum and hippocampal region. Disease onset occurs at 2 to 4 years with seizures, ataxia, myoclonus, psychomotor retardation, vision loss, and speech impairment. Enzyme replacement therapy for late infantile NCL (CLN2) is available to help slow progression of disease in children.

Diagnostic strategy depends on the age of onset of symptoms. In children presenting between 0 to 4 years, enzyme

assay of PPT1 and TPP1 is an appropriate first step. For other patients suspected of having an NCL, molecular genetic testing of CLN genes is available; see NCLGP / Neuronal Ceroid Lipofuscinosis (Batten Disease) Gene Panel, Varies.

Reference Values

Palmitoyl-protein thioesterase 1: >10.0 nmol/mL/h
Tripeptidyl peptidase 1: >27.0 nmol/mL/h

An interpretative report will be provided.

Interpretation

Abnormal results are not sufficient to establish a diagnosis of a particular disease. To verify a preliminary diagnosis based on this assay, additional biochemical or molecular genetic analyses are required.

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 genetic analysis), and a phone number to reach one of the laboratory directors in case the referring physician has additional questions.

Cautions

Deficiency of tripeptidyl peptidase 1 (*TPP1)* can also be indicative of autosomal recessive spinocerebellar ataxia-7.

Individuals with pseudodeficiency alleles can show reduced enzyme activity.

Carrier status (heterozygosity) for these conditions cannot be reliably detected.

Enzyme levels may be normal in individuals receiving enzyme replacement therapy or who have undergone hematopoietic stem cell transplant.

Clinical Reference

1. Hofmann SL, Peltonen L. The neuronal ceroid lipofuscinoses. In: Valle DL, Antonarakis S, Ballabio A, Beaudet AL, Mitchell GA. eds. The Online Metabolic and Molecular Bases of Inherited Disease. McGraw-Hill; Accessed September 2, 2025. Available at https://ommbid.mhmedical.com/content.aspx?bookid=2709&sectionid=225548100
2. Kohlschutter A, Schulz A, Bartsch U, Storch S. Current and emerging treatment strategies for neuronal ceroid lipofuscinoses. CNS Drugs. 2019;33(4):315-325. doi:10.1007/s40263-019-00620-8.
3. Schulz A, Specchio N, de Los Reyes E, et al. Safety and efficacy of cerliponase alfa in children with neuronal ceroid lipofuscinosis type 2 (CLN2 disease): an open-label extension study. Lancet Neurol. 2024;23(1):60-70. doi:10.1016/S1474-4422(23)00384-8

Performance

Method Description

One dried blood spot sample (DBS) is incubated with a mix of substrate and internal standard (IS) for iduronate 2-sulfatase, heparan N-sulfatase, alpha-N-acetylglucosaminidase, N-acetylgalactosamine-sulfate, beta-galactosidase,

arylsulfatase B, beta-glucuronidase, and tripeptidyl peptidase 1. A second DBS sample is incubated with a mix of substrate and IS for acetyl-CoA:alpha-glucosaminide N-acetyltransferase; and a third DBS sample with a mix of substrate and IS for palmitoyl-protein thioesterase 1. Following overnight incubation, the samples are combined, extracted by liquid-liquid extraction, and analyzed by tandem mass spectrometry.(Unpublished Mayo method)

PDF Report
No

Day(s) Performed
Thursday

Report Available
3 to 9 days

Specimen Retention Time
1 year

Performing Laboratory Location
Mayo Clinic Laboratories - Rochester Main Campus

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
82657

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
NCLBS	CLN1 and CLN2, BS	101348-1

Result ID	Test Result Name	Result LOINC® Value
BG757	Reason for Referral	42349-1
618435	Palmitoyl-protein thioesterase 1	59246-9
618436	Tripeptidyl peptidase 1	72498-9

618437	Interpretation	59462-2
618434	Reviewed By	18771-6