MAYO CLINIC LABORATORIES

Test Definition: NCLW

Neuronal Ceroid Lipofuscinosis, Two-Enzyme Panel, Leukocytes

Overview

Useful For

Supporting the biochemical diagnosis of two neuronal ceroid lipofuscinoses, CLN1 and CLN2 in whole blood specimens

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
- Informed Consent for Genetic Testing (Spanish)

Method Name

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

NY State Available

Yes

Specimen

Specimen Type

Whole Blood ACD

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.

Shipping Instructions

For optimal isolation of leukocytes, it is recommended the specimen arrive refrigerated within 6 days of collection to be stabilized. Pre-analytical processing is performed Monday through Friday and Sunday. This test may be canceled if specimens are outside of stability when processing occurs. Collect and package specimens for arrival on days when processing is performed.

Necessary Information

1. Patient's age is required.

2. Reason for testing is required.

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.

Specimen Minimum Volume

5 mL

Reject Due To

Gross hemolysis	Reject

Specimen Stability Information

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

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/h/mg protein
Tripeptidyl peptidase 1: >20.0 nmol/h/mg protein

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 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

Leukocytes are incubated with four cocktail mixes in 96-well plates: 1) 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; 2) substrate and IS for acetyl-CoA:alpha-glucosaminide N-acetyltransferase; 3) substrate and IS for N-acetylglucosamine-6-sulfatase; and 4) substrate and IS for palmitoyl-protein thioesterase 1. Following overnight incubation, the plates are combined and purified by liquid-liquid extraction. The extracts are evaporated, reconstituted with mobile phase, and analyzed by tandem mass spectrometry.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Preanalytical processing: Monday through Friday, Sunday
Testing performed: Tuesday

Report Available

3 to 9 days

Specimen Retention Time

WBC homogenate: 1 month

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
NCLW	CLN1 and CLN2, WBC	93704-5

Result ID	Test Result Name	Result LOINC® Value
BG773	Reason for Referral	42349-1
618471	Palmitoyl-protein thioesterase 1	74935-8
618472	Tripeptidyl peptidase 1	76038-9
618473	Interpretation	59462-2
618470	Reviewed By	18771-6