Overview

Useful For
Evaluation of patients with clinical presentations suggestive of neuronal ceroid lipofuscinoses (NCL)

Aids in the differential diagnosis of infantile and late infantile NCL

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

Special Instructions
- Informed Consent for Genetic Testing
- Biochemical Genetics Patient Information
- Informed Consent for Genetic Testing (Spanish)

Method Name
Fluorometric

NY State Available
Yes

Specimen

Specimen Type
Whole Blood ACD

Shipping Instructions
For optimal isolation of leukocytes, it is recommended the specimen arrive refrigerate within 144 hours of draw to be stabilized. Draw specimen Monday through Thursday only and not the day before a holiday. Specimen should be drawn 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)

Specimen Volume: 6 mL

Collection Instructions: Do not transfer blood to other containers.

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)
Test Definition: TPPTL
TPP1 and PPT1, WBC

- Informed Consent for Genetic Testing-Spanish (T826)

2. Biochemical Genetics Patient Information (T602) 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
5 mL

Reject Due To

| Gross hemolysis | Reject |

Specimen Stability Information

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Clinical and Interpretive

Clinical Information

The neuronal ceroid lipofuscinoses (NCL) comprise a group of recessively inherited neurodegenerative disorders involved in lysosomal protein catabolism. They are considered the most common of the neurogenetic storage disorders with incidences ranging from 1.3 to 7 per 100,000 live births. Clinically they are characterized by vision loss, seizures, mental regression, behavioral changes, movement disorders, and the accumulation of autofluorescent storage material in the brain and tissues. Although at least 12 different genes have been identified, the NCL have traditionally been categorized based on the age of onset of symptoms: infantile, late-infantile, juvenile, and adult. Infantile and late-infantile NCL are caused primarily by defects in \textit{PPT1} and \textit{TPP1}, respectively. Tissue damage is selective for the nervous system and many patients die in the first decade of life due to central nervous system degeneration.

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 of 2. 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 (GRODs) in most cell types. PPT1 is thought to play an active role in various cell processes including apoptosis, endocytosis, and lipid metabolism. Infantile NCL has an incidence of 1 in 20,000 in Finland and is rare elsewhere.

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 of age with seizures, ataxia, myoclonus, psychomotor retardation, vision loss, and speech impairment.
Diagnostic strategy depends on the age of onset of symptoms. In children presenting between the ages 0 to 4 years, enzyme assay of PPT1 and TPP1 is an appropriate first step. For other patients suspected of having an NCL, the molecular genetic test NCLP / Neuronal Ceroid Lipofuscinosis (NCL, Batten Disease) Panel by Next-Generation Sequencing is available.

**Reference Values**

TRIPEPTIDYL PEPTIDASE 1

85-326 nmol/hour/mg protein

PALMITOYL-PROTEIN THIOESTERASE 1

20-93 nmol/hour/mg protein

**Interpretation**

Tripeptidyl peptidase 1 (TPP1) and palmitoyl-protein thioesterase 1 (PPT1) enzyme activity below 5 nmol/hour/mg of protein are highly suggestive of late-infantile and infantile neuronal ceroid lipofuscinoses (NCL), respectively.

**Cautions**

This assay does not detect carrier status of neuronal ceroid lipofuscinoses (NCL).

Some variants with an age of onset occurring in older individuals have been noted.

**Clinical Reference**

1. Mole S, Cotman S: Genetics of the neuronal ceroid lipofuscinoses (Batten disease). Biochem et Biophys Acta 2015;1852:2237-2241


**Performance**

**Method Description**

The synthetic substrate for palmitoyl-protein thioesterase 1 (PPT1) is 4-methylumbelliferyl-6-thiopalmitoyl-beta-glucoside. The leukocytes are homogenized and combined with protein and a substrate and incubated. The reaction is stopped with a glycine buffer. The fluorescence of the 4-methylumbelliferone product is read using a fluorescence plate reader and activity is calculated based on amount of product formed during the 1-hour incubation period.(van Diggelen OP, Keulemans JL, Winchester B, et al: A rapid fluorogenic palmitoyl-protein thioesterase assay: Pre and postnatal diagnosis of INCL. Mol Genet Metab 1999;66:240-244)

The synthetic substrate for tripeptidyl peptidase 1 (TPP1) is Ala-Ala-Phe-7-amido-4-methylcoumarin. The leukocytes are homogenized and combined with protein and a substrate and incubated. The reaction is stopped with a glycine buffer. The fluorescence of the 7-amino-4-methylcoumarin product is read using a fluorescence plate reader and...
Test Definition: TPPTL
TPP1 and PPT1, WBC


PDF Report
No

Day(s) and Time(s) Test Performed
Specimens are processed Monday through Sunday.

Assay is performed: Varies

Analytic Time
8 days

Maximum Laboratory Time
15 days

Specimen Retention Time
WBC homogenate stored for 1 month

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
82657

LOINC® Information

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