

Overview

Useful For

Follow up for abnormal biochemical or electron microscopy results suspicious for neuronal ceroid lipofuscinoses (NCL)

Establishing a molecular diagnosis for patients with NCL

Identifying variations within genes known to be associated with NCL, allowing for predictive testing of at-risk family members

Genetics Test Information

This test utilizes next-generation sequencing to detect single nucleotide and copy number variants in 16 genes associated with neuronal ceroid lipofuscinosis (NCL/Batten Disease): *ATP13A2*, *CLN3*, *CLN5*, *CLN6*, *CLN8*, *CTSD*, *CTSF*, *CTSK*, *DNAJC5*, *GRN*, *KCTD7*, *MFSD8*, *PANK2*, *PPT1*, *SGSH*, *TPP1*. See [Targeted Genes and Methodology Details for Neuronal Ceroid Lipofuscinosis \(Batten Disease\) Gene Panel](#) in Special Instructions and Method Description for additional details.

Identification of a pathogenic variant may assist with diagnosis, prognosis, clinical management, familial screening, and genetic counseling for NCL (Batten disease).

Additional first tier testing may be considered/recommended. For more information see Ordering Guidance.

Special Instructions

- [Molecular Genetics: Biochemical Disorders Patient Information](#)
- [Informed Consent for Genetic Testing](#)
- [Informed Consent for Genetic Testing \(Spanish\)](#)
- [Targeted Genes and Methodology Details for Neuronal Ceroid Lipofuscinosis \(Batten Disease\) Gene Panel](#)

Method Name

Custom Sequence Capture and Targeted Next-Generation Sequencing followed by Polymerase Chain Reaction (PCR) and Sanger Sequencing

NY State Available

Yes

Specimen

Specimen Type

Varies

Ordering Guidance

[First-tier biochemical testing is available for the 2 most common types of enzyme deficiency associated with neuronal ceroid lipofuscinosis](#); order TPPTL / Tripeptidyl Peptidase 1 and Palmitoyl-Protein Thioesterase 1, Leukocytes.

Shipping Instructions

Specimen preferred to arrive within 96 hours of collection.

Specimen Required

Patient Preparation: A previous bone marrow transplant from an allogenic donor will interfere with testing. Call 800-533-1710 for instructions for testing patients who have received a bone marrow transplant.

Specimen Type: Whole blood

Container/Tube:

Preferred: Lavender top (EDTA) or yellow top (ACD)

Acceptable: Any anticoagulant

Specimen Volume: 3 mL

Collection Instructions:

1. Invert several times to mix blood.
2. Send specimen in original tube.

Specimen Stability Information: Ambient (preferred)/Refrigerated

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)

-[Informed Consent for Genetic Testing \(Spanish\)](#) (T826)

2. [Molecular Genetics: Biochemical Disorders Patient Information](#) (T527) in Special Instructions

Specimen Minimum Volume

See Specimen Required

Reject Due To

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Varies		

Clinical and Interpretive

Clinical Information

Neuronal ceroid lipofuscinoses (NCL) are a subset of lysosomal storage diseases that involve defective cellular processing of lipids. NCL are clinically characterized by epilepsy, intellectual and motor decline, and blindness.

Electron microscopy typically shows a characteristic accumulation of granular osmophilic deposits (GROD), curvilinear profiles (CVB), or fingerprint profiles (FP). Enzymatic testing may show deficiency in palmitoyl-protein thioesterase 1 (PPT1), tripeptidyl-peptidase 1 (TPP1), or cathepsin D (CTSD). Currently there are at least 14 genetically distinct forms.

Age of onset and clinical features can be variable, from congenital to adult onset. NCL is typically inherited in an autosomal recessive manner, although one adult onset form (ANCL; *DNAJC5* gene) has been shown to be autosomal dominant.

Reference Values

An interpretive report will be provided.

Interpretation

All detected alterations are evaluated according to American College of Medical Genetics and Genomics (ACMG) recommendations.⁽¹⁾ Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance.

Cautions

Clinical Correlations:

Test results should be interpreted in context of clinical findings, family history, and other laboratory data. Misinterpretation of results may occur if the information provided is inaccurate or incomplete.

If testing was performed because of a clinically significant family history, it is often useful to first test an affected family member. Detection of a reportable variant in an affected family member would allow for more informative testing of at risk individuals.

To discuss the availability of further testing options, for assistance in general test selection, or for assistance in the interpretation of these results, Mayo Clinic Laboratory genetic counselors can be contacted at 800-533-1710.

Technical Limitations:

Next-generation sequencing may not detect all types of genomic variants. In rare cases, false-negative or false-positive results may occur. The depth of coverage may be variable for some target regions, but assay performance below the minimum acceptable criteria or for failed regions will be noted. Given these limitations, negative results do not rule out the diagnosis of a genetic disorder. If specific clinical disorders are suspected, evaluation by alternative methods can be considered.

If the patient has had an allogeneic hematopoietic stem cell transplant or a recent heterologous blood transfusion, these results may be inaccurate due to the presence of donor DNA. Call Mayo Clinic Laboratories for instructions for testing patients who have received a bone marrow transplant.

There may be regions of genes that cannot be effectively amplified for sequencing or deletion and duplication analysis as a result of technical limitations of the assay, including regions of homology, high guanine-cytosine (GC) content, and repetitive sequences. Confirmation of select reportable variants will be performed by alternate methodologies based on internal laboratory criteria.

This assay will not reliably detect insertions/deletions (indels) of 40 or more base pairs (bp), including Alu insertions, long interspersed nuclear elements (LINES), and short interspersed nuclear elements (SINES). The bioinformatics software pipeline is verified to detect 95% of deletions up to 75 bp and insertions up to 47 bp.

Additionally, low level mosaic variants may not be detected.

This test is not designed to differentiate between somatic and germline variants. If there is a possibility that any detected variant is somatic, additional testing may be necessary to clarify the significance of results.

Reclassification of Variants-Policy:

At this time, it is not standard practice for the laboratory to systematically review previously classified variants on a regular basis. The laboratory encourages health care providers to contact the laboratory at any time to learn how the status of a particular variant may have changed over time.

Variant Evaluation:

Evaluation and categorization of variants is performed using published American College of Medical Genetics and Genomics (ACMG) and Association for Molecular Pathology (AMP) recommendations as a guideline. Other gene specific guidelines may also be considered. Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance. Variants classified as benign or likely benign are not reported.

Multiple in silico evaluation tools may be used to assist in the interpretation of these results. The accuracy of predictions made by in silico evaluation tools is highly dependent upon the data available for a given gene, and periodic updates to these tools may cause predictions to change over time. Results from in silico evaluation tools should be interpreted with caution and professional clinical judgment. Intronic and synonymous sequence variants not predicted to impact splicing or otherwise contribute to disease are not reported.

Clinical Reference

1. Richards S, Aziz N, Bale S, et al: Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. *Genet Med.* 2015 May;17(5):405-424
2. Mole SE, Cotman SL: Genetics of the neuronal ceroid lipofuscinoses (Batten disease). *Biochim Biophys Acta.* 2015;1852(10PtB):2237-2241
3. Cooper JD, Tarczyk MA, Nelvagal HR: Towards a new understanding of NCL pathogenesis. *Biochim Biophys Acta.* 2015;1852(10PtB):2256-2261
4. Williams RE, Mole SE: New nomenclature and classification scheme for the neuronal ceroid lipofuscinoses. *Neurology.* 2012;79(2):183-191
5. Mole SE, Williams RE: Neuronal ceroid-lipofuscinoses. In: Adam MP, Ardinger HH, Pagon RA, et al, eds. *GeneReviews* [Internet]. University of Washington. , Seattle; 2001. Updated August 1, 2013. Accessed October 28, 2020. Available at www.ncbi.nlm.nih.gov/books/NBK1428/

Performance

Method Description

Next generation sequencing (NGS) and/or Sanger sequencing is performed to test for the presence of variants in coding regions and intron/exon boundaries of the genes analyzed. NGS and/or a polymerase chain reaction (PCR)-based quantitative method is performed to test for the presence of deletions and duplications in the genes analyzed.

There may be regions of genes that cannot be effectively amplified for sequencing or deletion and duplication analysis as a result of technical limitations of the assay, including regions of homology, high guanine-cytosine (GC)

content, and repetitive sequences. Confirmation of select reportable variants may be performed by alternate methodologies based on internal laboratory criteria.

PCR-based methods and/or Sanger sequencing is used to confirm variants detected by NGS when appropriate. (Unpublished Mayo method)

[See Targeted Genes and Methodology Details for Neuronal Ceroid Lipofuscinosis \(Batten Disease\) Gene Panel](#) in Special Instructions for details regarding the targeted gene regions for this test.

Genes analyzed: *ATP13A2*, *CLN3*, *CLN5*, *CLN6*, *CLN8*, *CTSD*, *CTSF*, *CTSK*, *DNAJC5*, *GRN*, *KCTD7*, *MFSD8*, *PANK2*, *PPT1*, *SGSH*, *TPP1*

PDF Report

No

Day(s) Performed

Varies

Report Available

3 to 4 weeks

Specimen Retention Time

Whole Blood: 2 weeks (if available); Extracted DNA: 3 months

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

81443

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
NCLGP	NCL (Batten Disease) Gene Panel	In Process



Result ID	Test Result Name	Result LOINC Value
608572	Test Description	62364-5
608573	Specimen	31208-2
608574	Source	31208-2
608575	Result Summary	50397-9
608576	Result	82939-0
608577	Interpretation	69047-9
608578	Resources	In Process
608579	Additional Information	48767-8
608580	Method	85069-3
608581	Genes Analyzed	48018-6
608582	Disclaimer	62364-5
608583	Released By	18771-6