Neuronal Ceroid-Lipofuscinoses: Deletion/Duplication Panel  

**Condition Description**

As a group, the neuronal ceroid-lipofuscinoses (NCL and also known as Batten disease) are progressive autosomal recessive lysosomal storage disorders causing neurodegenerative disease. The clinical spectrum is characterized by vision loss, seizures, cognitive decline, motor decline, and early demise. The clinical spectrum can be divided into the following phenotypes based on age of onset and symptom presentation: infantile; late-infantile; juvenile; adult; and Northern epilepsy. Both genetic and allelic heterogeneity exist and current classifications are made using the gene and age at symptom presentation. The classic late infantile form (CLN2 disease) presents between two and four years of age with seizures and ataxia followed by cognitive and motor decline. Vision also deteriorates and a tapeto-retinal degeneration eventually causes blindness. The clinical course typically results in a life expectancy from six years to adolescence. In the classic juvenile form (CLN3 disease), the first clinical sign, typically evident between four and ten years of age, is retinitis pigmentosa resulting in decreased central vision and complete blindness eventually follows. Cognitive decline is apparent usually by age ten and insomnia is common with seizures following in subsequent years. Additionally, speech disturbances, a Parkinsonian-like gate, depression, agitation and hallucinations are some of the common clinical features. Worsening seizures are evident with disease progression and individuals may survive into their 30s.

Please note that the DNAJC5 gene, identified in adult onset autosomal dominant NCL, is not included in this NGS panel due to the presence of at least one pseudogene. For clinicians that suspect autosomal dominant NCL and would like DNAJC5 analysis in the event that all other genes test negative, we request that you contact the EGL directly.


**References:**

- OMIM
- GeneReviews
- Emory and Rimoin's Principles and Practice of Medical Genetics, 5th Edition

**Genes**

ATP13A2, CLN3, CLN5, CLN6, CLN8, CTSD, GRN, KCTD7, MFSD8, PPT1, TPP1

**Indications**

This test is indicated for:

- Confirmation of a clinical diagnosis of NCL.
- Carrier testing in adults with a family history of NCL.

**Methodology**

**Deletion/Duplication Analysis:** DNA isolated from peripheral blood is hybridized to a gene-targeted CGH array to detect deletions and duplications. The targeted CGH array has overlapping probes that cover the entire genomic region.

Please note that a "backbone" of probes across the entire genome are included on the array for analytical and quality control purposes. Rarely, off-target copy number variants causative of disease may be identified that may or may not be related to the patient's phenotype. Only known pathogenic off-target copy number variants will be reported. Off-target copy number variants of unknown clinical significance will not be reported.

**Detection**

**Deletion/Duplication:** Detection is limited to duplications and deletions. The CGH array will not detect point or intronic pathogenic variants. Results of molecular analysis must be interpreted in the context of the patient's clinical and/or biochemical phenotype.

**Specimen Requirements**

Submit only 1 of the following specimen types

**Type: Whole Blood**

Specimen Requirements:

- In EDTA (purple top) tube:
  - Infants (2 years): 3-5 ml
  - Older Children & Adults: 5-10 ml.

Specimen Collection and Shipping: Refrigerate until time of shipment. Ship sample within 5 days of collection at room temperature with overnight
Type: Isolated DNA

Specimen Requirements:

In microtainer: 10 ug

Isolation using the Qiagen™ Puregene kit for DNA extraction is recommended.

Specimen Collection and Shipping:

**Special Instructions**

Please include fundus photographs, electroretinogram (ERG) findings, visual field findings, and visual acuity, if available, for expert review and clinical correlation with test results.

**Related Tests**

- Neuronal Ceroid-Lipofuscinoses: Sequencing Panel
- Eye Disorder: Comprehensive Sequencing
- Eye Disorder: Deletion/Duplication Panel