Niemann-Pick Disease Type C: **NPC1 & NPC2 Gene Deletion/Duplication**

**Test Code:** NE  
**Turnaround time:** 2 weeks  
**CPT Codes:** 81228 x1

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### Condition Description

Niemann-Pick Disease, Type C (NPD-C) is an autosomal recessive lipid storage disorder caused by a defect in esterification of exogenously derived low-density lipoprotein cholesterol. This impairment in the transport of cholesterol and glycosphingolipids leads to the accumulation of cholesterol in the lysosomes[1,2]. The accumulation of lipids in lysosomes leads to engorged lysosomes, deficiencies in membrane cholesterol, and eventually cell death. NPD-C can present at any stage in life. Infants may present with severe liver disease, organomegaly, pulmonary disease, hypotonia, and developmental delay. Idiopathic neonatal cholestatis is considered a significant indicator of NPD-C. Typical presentation in older children may present with ataxia, vertical and horizontal supranuclear gaze palsy, dementia, dystonia, enlarged liver and spleen, and seizures. As the disease progresses, patients have difficulty coordinating the muscles for eating, walking, and speaking. In the adult onset form of the disease, affected individuals typically present with dementia and psychiatric symptoms. The biochemical diagnosis is made by evaluating LDL-cholesterol esterification in cultured fibroblasts and filipin staining showing accumulation of unesterified cholesterol. Mutations in the **NPC1** and **NPC2** genes are responsible for NPD-C. Complementation studies indicate that the vast majority of individuals with NPD-C have mutations in the **NPC1** gene[3] with ~4% of cases mutations having mutations in the **NPC2** gene[4]. Although there is a common **NPC1** mutation found in individuals of Mexican descent in the Rio Grande valley and a common **NPC2** mutation found in individuals from Nova Scotia, there are over 200 other mutations have been identified in the **NPC1** and **NPC2** genes. The majority of **NPC1** and **NPC2** mutations are private missense mutations [4-6]. For questions about testing for NPD-C disease, call EGL Genetics at (470) 378-2200 or (855)831-7447. For further clinical information about lysosomal storage diseases, including management and treatment, call the Emory Lysosomal Storage Disease Center at (404) 778-8565 or (800) 200-1524.

### References:

### Genes
**NPC1, NPC2**

### Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of Niemann-Pick Disease, Type C
- Prenatal testing for known familial mutations.
- Carrier testing in adults with a family history of Niemann-Pick Disease, Type C in whom sequence analysis was negative.

### Methodology

DNA isolated from peripheral blood is hybridized to a CGH array to detect deletions and duplications. The targeted CGH array has overlapping probes which cover the entire genomic region.

### Detection

Detection is limited to duplications and deletions. Array CGH will not detect point mutations or intronic mutations. 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 (EDTA)**

**Specimen Requirements:**

**EDTA (Purple Top)**  
Infants and Young Children (2 years of age to 10 years old): 3-5 ml  
Older Children & Adults: 5-10 ml  
Autopsy: 2-3 ml unclotted cord or cardiac blood

**Specimen Collection and Shipping:**  
Ship sample at room temperature for receipt at EGL within 72 hours of collection. Do not freeze.
Type: DNA, Isolated

Specimen Requirements:
- Microtainer
- 3µg

Isolation using the Perkin Elmer™ Chemagen™ Automated Extraction method or Qiagen™ Puregene kit for DNA extraction is recommended.

Specimen Collection and Shipping:
Refrigerate until time of shipment in 100 ng/µL in TE buffer. Ship sample at room temperature with overnight delivery.

Special Instructions
Submit copies of diagnostic biochemical test results with the sample. Sequence analysis is required before deletion/duplication analysis by targeted CGH array. If sequencing is performed outside EGL Genetics, please submit a copy of the sequencing report with the test requisition. Contact the laboratory if further information is needed.

Related Tests
- Mucopolysaccharide Screen (Urine GAG) (GA)
- Known Mutation Analysis (KM) is available to test family members.
- Prenatal testing is available for known familial mutations only. Please call the Laboratory Genetic Counselor for specific requirements for prenatal testing before collecting a fetal sample.