NSDHL-related Disorders: NSDHL Gene Deletion/Duplication

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

### Condition Description

**CK Syndrome**  
Intellectual disability (ID) is a nonprogressive cognitive impairment affecting 1-3% of the Western population. It is estimated that up to 50% of moderate-severe cases have genetic causes and approximately 10% are due to X-linked intellectual disability disorders (XLID). XLID can be syndromic or nonsyndromic and is observed in all ethnic groups. More than 100 XLID syndromes have been described in the literature to date. Fragile X is the most common XLID syndrome (~1 in 4000 males) while others can be quite rare with only a few patients reported in the literature. Males can have moderate to severe intellectual disability depending on the syndrome, and carrier females can also be affected, but typically have milder clinical symptoms.

**CHILD syndrome**  
Loss of function mutations in the NSDHL gene cause congenital hemidysplasia with ichthyosiform nevus and limb defects (CHILD) syndrome. CHILD syndrome is X-linked dominant with lethality in males and is characterized by unilateral distribution of ichthyosiform nevus, limb defects that are ipsilateral to the skin lesions, punctuate calcification of cartilaginous structures, visceral malformation, and central nervous system anomalies. Additionally, heart defects, lung hypoplasia and renal findings have been reported. Intellect is usually normal.

References:  
- GeneReviews  
- OMIM #300275: NSDHL gene  
- OMIM #308050: CHILD syndrome  
- OMIM #308300: CK syndrome

### Genes

- **NSDHL**

### Indications

This test is indicated for:  
- Confirmation of a clinical diagnosis of NSDHL-Related Disorders in individuals who have tested negative for sequence analysis.  
- Carrier testing in adults with a family history of NSDHL-Related Disorders who have tested negative for sequence analysis.

### 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. The CGH array will not detect point 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
Sequence analysis is required before deletion/duplication analysis by targeted CGH array. If sequencing is performed outside of EGL Genetics, please submit a copy of the sequencing report with the test requisition.

Related Tests
- Sequence analysis of the NSDHL gene is available and is required before deletion/duplication analysis.
- Prenatal testing is available to couples who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.
- X-Linked Intellectual Disability panels are available for 30, 60, and 90 genes.