**NSDHL-related Disorders: NSDHL Gene Sequencing**

**Test Code:** SNSDH  
**Turnaround time:** 4 weeks  
**CPT Codes:** 81479 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.

CK syndrome, an X-linked recessive condition, is characterized by ID; central nervous system findings, including microcephaly and seizures; craniofacial features; and asthenic habitus. Mutations in the *NSDHL* gene (Xq28) cause CK syndrome. Female carrier relatives of a male with CK syndrome are clinically unaffected.

**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

## Methodology

PCR amplification of 7 exons contained in the *NSDHL* gene is performed on the patient's genomic DNA. Direct sequencing of amplification products is performed in both forward and reverse directions, using automated fluorescence dideoxy sequencing methods. The patient's gene sequences are then compared to a normal reference sequence. Sequence variations are classified as mutations, benign variants unrelated to disease, or variations of unknown clinical significance. Variants of unknown clinical significance may require further studies of the patient and/or family members. This assay does not interrogate the promoter region, deep intronic regions, or other regulatory elements, and does not detect large deletions.

**Detection**

Clinical Sensitivity: Unknown. Mutations in the promoter region, some mutations in the introns and other regulatory element mutations cannot be detected by this analysis. Large deletions will not be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's biochemical phenotype.

Analytical Sensitivity: ~99%

## Specimen Requirements

Submit only 1 of the following specimen types

* Preferred specimen type: Whole Blood

**Type: Whole Blood**

Specimen Requirements:

In EDTA (purple top) or ACD (yellow 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 delivery.

**Type: Saliva**

Specimen Requirements:

Oragene™ Saliva Collection kit (available through EGL) used according to manufacturer instructions.

Specimen Collection and Shipping: Store sample at room temperature. Ship sample within 5 days of collection 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 Emory Genetics Laboratory, please submit a copy of the sequencing report with the test requisition.

**Related Tests**

- Deletion/duplication analysis of the NSDHL gene by CGH array is available for those individuals in whom sequence analysis is negative.
- Custom diagnostic mutation analysis (KM) is available to family members if mutations are identified by targeted mutation testing or sequencing analysis.
- Prenatal testing is available only for known familial mutations to individuals 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.