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.

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

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.

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
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
* 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

- 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.