Cornelia de Lange Syndrome: *NIPBL* Gene Deletion/Duplication

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

### Condition Description

Mutations in three genes, *NIPBL* (5p13.1), *SMC1A*, and *SMC3* are currently reported to cause Cornelia de Lange syndrome (CdLS). Mutations in the *NIPBL* gene more often cause the classical form of CdLS, while mutations in the *SMC1A* and *SMC3* genes often cause a more mild form of CdLS. Classical CdLS is characterized by distinctive facial features (including microbryophthalmia, arched eyebrows, long, thick eyelashes, low-set posteriorly rotated and/or hirsute ears with thickened helices, depressed or broad nasal bridge, long smooth philtrum, low arched or cleft palate, small widely-spaced teeth, micrognathia, and a short neck), growth retardation, hirsuitism, and upper limb reduction deficits. Additional features include intellectual disability, cardiac defects, gastrointestinal dysfunction, hearing loss, myopia, and hypoplastic genitalia. Individuals with a milder phenotype have less severe growth, cognitive, and limb involvement but usually have the classical facial features associated with CdLS.

Please note that this test if for the *NIPBL* gene only. For patients with suspected CdLS, sequence analysis is recommended as the first step in mutation identification. For patients in whom mutations are not identified by full gene sequencing, deletion/duplication analysis is appropriate.


### References:
- GeneReviews
- OMIM #608667: *NIPBL* gene
- OMIM #122470: CdLS

### Genes

**NIPBL**

### Indications

This test is indicated for:
- Confirmation of a clinical diagnosis of Cornelia de Lange syndrome in an individual in whom sequence analysis was negative.
- Carrier testing in adults with a family history of Cornelia de Lange syndrome 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.

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) 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 EGL Genetics, please submit a copy of the sequencing report with the test requisition.

**Related Tests**

- Sequence analysis of the NIPBL gene is available and is required before deletion/duplication analysis.
- 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.

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