**Condition Description**

Mutations in five genes, **HDAC8**, **NIPBL** (5p13.1), **RAD21**, **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 **HDAC8**, **RAD21**, **SMC1A**, and **SMC3** genes often cause a more mild form of CdLS. Classical CdLS is characterized by distinctive facial features (including microbrachycephaly, arched eyebrows, long, thick eyelashes, low-set posteriorly rotated and/or hirsute ears with thickened helices, depressed or broad nasal bridge, long smooth philtrum, high arched or cleft palate, small widely-spaced teeth, micrognathia, and a short neck), growth retardation, hirsutism, 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.


**References:**

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

**Genes**

**HDAC8**, **NIPBL**, **RAD21**, **SMC1A**, **SMC3**

**Indications**

This test is indicated for:

- Confirmation of a clinical diagnosis of Cornelia de Lange syndrome.
- Carrier testing in adults with a family history of Cornelia de Lange syndrome.

**Methodology**

**Deletion/Duplication Analysis:** 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**

**Deletion/Duplication Analysis:** 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**

Specimen Requirements:

- In EDTA (purple top) tube:
  - Infants (2 years): 3-5 ml
  - Older Children & Adults: 5-10 ml

Specimen Collection and Shipping: Ship sample at room temperature with overnight delivery.

**Type: Isolated DNA**

Specimen Requirements:

- In microtainer: 10 ug

Isolation using the Qiagen™ Puregene kit for DNA extraction is recommended.
Specimen Collection and Shipping: Refrigerate until time of shipment in 100 ng/ul of TE buffer. Ship sample at room temperature with overnight delivery.

**Related Tests**

- Cornelia de Lange Syndrome: Sequencing Panel
- *NIPBL* Sequencing and deletion/duplication analysis
- *SMC1A* Sequencing and deletion/duplication analysis