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 milder form of CdLS. Classical CdLS is characterized by distinctive facial features (including microcephaly, 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.

Please note that this test is 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.

Visit [www.ThinkGenetic.com](http://www.ThinkGenetic.com) for patient-friendly information on **Cornelia de Lange syndrome**.

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.

**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 24 hours of collection. Do not refrigerate or freeze.

**Type: DNA, Isolated**

**Specimen Requirements:**
- Microtainer
- 3μg
- Isolation using the Perkin Elmer™Chemagen™ 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 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.