Cornelia de Lange Syndrome: SMC1A Gene Deletion/Duplication

Test Code: DSMC1
Turnaround time: 2 weeks
CPT Codes: 81228 x1

Condition Description

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.

Mutations in three genes, NIPBL, SMC1A (Xp11.22-p11.21), 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 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 defects. 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 SMC1A gene only.


References:
GeneReviews
OMIM #300040: SMC1A gene
OMIM #300590: CdLS

Genes

SMC1A

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™ 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 SMC1A 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.
- X-Linked Intellectual Disability panels are available for 30, 60, and 90+ genes.