X-linked Opitz G/BBB Syndrome: MID1 Gene Deletion/Duplication

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

Condition Description

X-linked Opitz G/BBB syndrome is a congenital midline malformation syndrome characterized by facial anomalies, laryngo-tracheo-esophageal defects, and genitourinary abnormalities. Facial anomalies seen in X-linked Opitz G/BBB syndrome include ocular hypertelorism, prominent forehead, widow's peak, broad nasal bridge, and anteverted nares. Genitourinary abnormalities include hypospadias, cryptorchidism, and hypoplastic/bifid scrotum. The condition is genetically heterogeneous, as there is an autosomal dominant form as well.

Hypertelorism and hypospadias are the most frequent manifestations of X-linked Opitz G/BBB syndrome, being present in almost all individuals. Developmental delay and mental retardation are observed in about 50% of affected males. Cleft lip and/or palate are present in approximately 50% of affected individuals. Other malformations present in fewer than 50% of individuals include congenital heart defects, imperforate or ectopic anus, and midline brain defects (Dandy-Walker malformation and agenesis or hypoplasia of the corpus callosum or cerebellar vermis). Monozygotic twinning is unusually frequent in families of individuals with X-linked Opitz G/BBB syndrome, and may be a manifestation of the defect; unusually severe cases with early lethality occur as twins. Wide clinical variability occurs even among members of the same family. Female carriers usually manifest only ocular hypertelorism. The prevalence of X-linked Opitz G/BBB syndrome ranges from one in 50,000 to one in 100,000 males.

The diagnosis of X-linked Opitz G/BBB syndrome is established most often by clinical findings. MID1 (Xp22) is the only gene currently known to be associated with X-linked Opitz G/BBB syndrome. Sequence analysis of the MID1 gene detects mutations in 15%-45% of males with clinically diagnosed Opitz G/BBB syndrome. Deletions and duplications in and of the MID1 gene have also been reported. The cohorts tested for MID1 mutations often include simplex cases (i.e., individuals with no family history of Opitz G/BBB syndrome), who therefore cannot be determined to have either the X-linked form or the autosomal dominant form. The detection rate is higher in individuals with clear X-linked inheritance. De novo mutations have been reported.

Click here for the GeneTests summary on this condition.

Genes

MID1

Indications

This test is indicated for:

- Confirmation of a clinical/biochemical diagnosis of X-linked Opitz G/BBB syndrome in individuals who have tested negative for sequence analysis
- Carrier testing in adult females with a family history of X-linked Opitz G/BBB syndrome 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.

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 72 hours of collection. Do not 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
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

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.

Related Tests

- Sequencing analysis of the MID1 gene is available (ZC) and is required before deletion/duplication analysis.
- ACGH array-based test for deletion/duplication analysis of 64 different X-linked intellectual disability genes is available (OL).
- Prenatal testing is available to adult females who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.