X-linked Opitz G/BBB Syndrome: \textit{MID1} Gene Deletion/Duplication

\textbf{Test Code: ZD}
\textbf{Turnaround time: 2 weeks}
\textbf{CPT Codes: 81228 x1}

\section*{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 and/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. \textit{MID1} (Xp22) is the only gene currently known to be associated with X-linked Opitz G/BBB syndrome. Sequence analysis of the \textit{MID1} gene detects mutations in 15%-45% of males with clinically diagnosed Opitz G/BBB syndrome. Deletions and duplications in and of the \textit{MID1} gene have also been reported. The cohorts tested for \textit{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. \textit{De novo} mutations have been reported.

\textbf{Genes}

\textit{MID1}

\section*{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

\section*{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.

\section*{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.

\section*{Specimen Requirements}

Disclaimer: This information is confidential and subject to change without notice. It may not be reproduced in whole or part unless authorized in writing by an authorized EGL representative.
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**

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.
- A CGH 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.