XLMR with Agenesis of the Corpus Callosum: *IGBP1* Gene Deletion/Duplication

**Condition Description**

In 2003, Graham et al. reported two brothers with a unique clinical presentation and mutations in the *IGBP1* gene (Xq13.1-q13.3), also called the Alpha 4 gene.

The brothers had a clinical presentation of coloboma (iris in one brother and optic nerve in the other), high forehead, severe retrognathia, mild to moderate intellectual disability, and agenesis of the corpus callosum (ACC). They also had low-set cupped ears with sensorineural hearing loss, downslanting palpebral fissures, short broad neck, pectus excavatum, scoliosis, and short stature. One brother also had choanal atresia and cardiac defects (ventricular septal defect and patent ductus arteriosus).

Changes in the 5' UTR sequence of the *IGBP1* gene were identified in these brothers and their carrier mother. The changes were not observed in the brothers' maternal half-uncle or in 410 control chromosomes. The protein product of the *IGBP1* gene has been shown to interact with MID1, the product of the gene mutated in X-linked Opitz GBBB syndrome.

For patients with suspected XLMR with agenesis of the corpus callosum, 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.

**References:**

- OMIM #300472 Corpus Callosum, Agenesis of, with Mental Retardation, Ocular Coloboma, and Micrognathia

**Indications**

- Confirmation of a clinical diagnosis of X-linked agenesis of the corpus callosum with mental retardation, coloboma, and micrognathia in an individual in whom sequence analysis was negative.
- Carrier testing in adult females with a family history of X-linked agenesis of the corpus callosum with mental retardation, coloboma, and micrognathia 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.

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**

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

* 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**

Submit copies of diagnostic biochemical test results with the sample, if appropriate. Contact the laboratory if further information is needed.

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 IGBP1 gene is available and is required before deletion/duplication analysis.
- An XLID sequencing panel and a CGH array-based test for deletion/duplication analysis of 90+ different X-linked intellectual disability genes are available.
- 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 for known familial mutations only. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.