XLMR with Agenesis of the Corpus Callosum: \textit{IGBP1} Gene Sequencing

**Test Code:** SIGBP  
**Turnaround time:** 6 weeks  
**CPT Codes:** 81479 x1

### Condition Description

In 2003, Graham et al. reported two brothers with a unique clinical presentation and mutations in the \textit{IGBP1} gene (Xq13.1-q13.3), also called the \textit{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 \textit{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 \textit{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](https://omim.org/entry/300472)

### Genes

\textit{IGBP1}

### Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of X-linked agenesis of the corpus callosum with mental retardation, coloboma, and micrognathia.
- Carrier testing in adult females with a family history of X-linked agenesis of the corpus callosum with mental retardation, coloboma, and micrognathia.

### Methodology

PCR amplification of 6 exons contained in the \textit{IBGP1} gene is performed on the patient's genomic DNA. Direct sequencing of amplification products is performed in both forward and reverse directions, using automated fluorescence dideoxy sequencing methods. The patient's gene sequences are then compared to a normal reference sequence. Sequence variations are classified as mutations, benign variants unrelated to disease, or variations of unknown clinical significance. Variants of unknown clinical significance may require further studies of the patient and/or family members. This assay does not interrogate the promoter region, deep intronic regions, or other regulatory elements, and does not detect large deletions.

### Detection

Clinical Sensitivity: Unknown. Mutations in the promoter region, some mutations in the introns and other regulatory element mutations cannot be detected by this analysis. Large deletions will not be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's biochemical phenotype.

Analytical Sensitivity: \(~99\%\)

### Specimen Requirements

Submit only 1 of the following specimen types

* Preferred specimen type: Whole Blood

**Type: Whole Blood**

Specimen Requirements:

In EDTA (purple top) or ACD (yellow 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 Emory Genetics Laboratory, please submit a copy of the sequencing report with the test requisition.

### Related Tests

- Deletion/duplication analysis of the *IGBP1* gene by CGH array is available for those individuals in whom sequence analysis is negative.
- 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.