

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

Test Code: DIGBP

Turnaround time: 2 weeks

CPT Codes: 81228 x1

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:

- Graham, JM et al. A new X-linked syndrome with agenesis of the corpus callosum, mental retardation, coloboma, micrognathia, and a mutation in the Alpha 4 gene at Xq13. *Am J Med Gen* 2003; 123A:37-44.
- OMIM #300472 [Corpus Callosum, Agenesis of, with Mental Retardation, Ocular Coloboma, and Micrognathia](#)

Genes

[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 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.

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™ 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

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.