MED12-related Disorders: MED12 Gene Deletion/Duplication

Test Code: DMED1  
Turnaround time: 2 weeks  
CPT Codes: 81228 x1

Condition Description

Intellectual disability (ID) is a nonprogressive cognitive impairment affecting 1-3% of the Western population. It is estimated that up to 50% of moderate-severe cases have genetic causes and approximately 10% are due to X-linked intellectual disability disorders (XLID). XLID can be syndromic or nonsyndromic and is observed in all ethnic groups. More than 100 XLID syndromes have been described in the literature to date. Fragile X is the most common XLID syndrome (~1 in 4000 males) while others can be quite rare with only a few patients reported in the literature. Males can have moderate to severe intellectual disability depending on the syndrome, and carrier females can also be affected, but typically have milder clinical symptoms.

FG Syndrome Type 1
FG syndrome type 1 (FGS1) is clinically diagnosed when six of the following eight features are present: intellectual disability, hypotonia, constipation and/or anal anomalies, small and simple ears, tall and prominent forehead, downslanting palpebral fissures, broad thumbs and halluces, and abnormalities of the corpus callosum. Additional features that can be seen in individuals with FGS1 are friendly, hyperactive, attention-seeking behavior; macrocephaly; and hypertelorism. FGS1 is caused by a recurrent p.ARG961Trp mutation in the MED12 gene (Xq13).

Lujan Syndrome
Lujan syndrome is clinically diagnosed when six of the following eight features are present: intellectual disability, hypotonia, macrocephaly, tall, thin body habitus, long, thin face, high nasal root, high narrow palate, and short philtrum. Additional features that can be seen in individuals with Lujan syndrome are hypernasal speech, micrognathia, hyperextensible digits, and abnormalities of the corpus callosum. Lujan syndrome is caused by a recurrent p.Asn1007Ser mutation in the MED12 gene (Xq13).

Female carriers could develop clinical findings related to the disorders.

For patients with a suspected MED12-Related Disorder, 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:

- GeneReviews
- OMIM #300188: MED12 gene
- OMIM #305450: FGS1
- OMIM #309520: Lujan syndrome

Genes

MED12

Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of MED12-Related Disorders in an individual in whom sequence analysis was negative.
- Carrier testing in adults with a family history of MED12-Related Disorders 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

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 clinical and/or biochemical phenotype.

Analytical Sensitivity: ~99%

Specimen Requirements

Submit only 1 of the following specimen types

Type: DNA, Isolated

Specimen Requirements:

Microtainer
3µg Isolation using the Perkin Elmer™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.

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 24 hours of collection. Do not refrigerate or freeze.

Special Instructions
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 MED12 gene by CGH array is available and is required before deletion/duplication analysis.
- 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 only for known familial mutations to individuals who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.
- X-Linked Intellectual Disability panels are available for 30, 60, and 90 genes.