**MED12-related Disorders: MED12 Gene Sequencing**

<table>
<thead>
<tr>
<th>Test Code: SMED1</th>
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<td>Turnaround time: 6 weeks</td>
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<td>CPT Codes: 81479 x1</td>
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**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).

**Genes**

**MED12**

**Indications**

This test is indicated for:

- Confirmation of a clinical diagnosis of MED12-Related Disorders.
- Carrier testing in adults with a family history of MED12-Related Disorders.

**Methodology**

**Next Generation Sequencing:** In-solution hybridization of all coding exons is performed on the patient's genomic DNA. Although some deep intronic regions may also be analyzed, this assay is not meant to interrogate most promoter regions, deep intronic regions, or other regulatory elements, and does not detect single or multi-exon deletions or duplications. Direct sequencing of the captured regions is performed using next generation sequencing. The patient's gene sequences are then compared to a standard reference sequence. Potentially causative variants and areas of low coverage are Sanger-sequenced. Sequence variations are classified as pathogenic, likely pathogenic, benign, likely benign, or variants of unknown significance. Variants of unknown significance may require further studies of the patient and/or family members.

**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

* 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

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

- Deletion/duplication analysis of the MED12 gene by CGH array is available for those individuals in whom sequence analysis is negative.
- 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.