

Lujan Syndrome / FG Syndrome Type 1 via *MED12* Gene Sequencing (Test #398)

Brief Description of Clinical Features: Lujan Syndrome (LS; also known as Lujan-Fryns Syndrome; OMIM 309520) and FG Syndrome Type 1 (FGS1; also known as Opitz-Kaveggia Syndrome; OMIM 305450) are allelic disorders with overlapping clinical phenotype. LS and FGS1 share the clinical findings of cognitive impairment and hypotonia (Lyons et al. J Med Genet 46:9-13, 2009). However, LS is further characterized by a Marfan-like appearance, which include marfanoid habitus (large head; tall, thin body habitus) and craniofacial changes (long, thin face; high nasal root; high, narrow palate; and short philtrum) (Lujan Am J Med Genet 17:311-322, 1984; Schwartz et al. J Med Genet 44:472-477, 2007). Conversely, FGS1 is further characterized by constipation, anal anomalies, small and simple ears, tall and prominent forehead, downslanting palpebral fissures, broad thumbs and halluces, and abnormalities of the corpus callosum (Opitz et al. Z Kinderheilkd. 117:1-18, 1974; Risheg et al. Nat Genet 39:451-453, 2007).

In addition, LS has overlapping clinical features with Loeys-Dietz syndrome (LDS, OMIM 609192; 608967; 610380; 610168), Shprintzen-Goldberg syndrome (OMIM# 182212), Fragile X syndrome (OMIM 300624) and Snyder-Robinson syndrome (OMIM 309583). While FGS1 has overlapping clinical features with alpha-thalasemia X-linked mental retardation syndrome (ATRX; OMIM 301040), Coffin-Lowry syndrome (OMIM 303600), Rubinstein-Taybi syndrome (OMIM 180849) and Fragile X syndrome (OMIM 300624).

Genetics: LS and FGS1 are both inherited in an X-linked recessive manner. Schwartz et al. (2007) reported that the c.3020A>G (p.Asn1007Ser) mutation in exon 22 of the *MED12* gene causes LS, while Risheg et al. (2007) reported that the c.2881C>T (p.Arg961Trp) mutation in exon 21 of *MED12* causes FGS1. *MED12* encodes the MED12 protein, a mediator of RNA polymerase II transcription subunit 12, which serves as an interface between transcription factors and RNA polymerase II. The mediator complex comprises 25 subunits organized into four modules. The MED12 protein is part of the module needed for repression of transcription (Zhou et al. Mol Cell Biol 26:8667-8682, 2006; Philibert and Madan Pharmacogenomics 8:909-916, 2007).

Description of this Particular Test: This test involves bidirectional DNA sequencing of all coding exons (1-45) of the *MED12* gene along with ~50 bases of non coding flanking DNA on each side. This test will start with sequencing exons 21 and 22, and only if these are negative will the remaining exons will be sequenced. As indicated, we will also perform sequencing of any single exon (our Test #100) or pair of exons (our Test #200) in this gene (\$190-340 charge).

Reference Sequences: Genomic: NC_000023.10 mRNA: NM_005120.1 Protein: NP_005111.2 (CCDS 43970.1)

Indications for Test: Candidates for this test are male patients with symptoms consistent with FG or LS and family members of patients who have known *MED12* mutations (Battaglia et al. Am J Med Genet 140:2075-9, 2006).

Sensitivity of Test: The prevalence of FGS and LS is unknown. *MED12* mutations have been identified in approximately 13% of individuals clinically diagnosed with FGS (Risheg et al. 2007).

Turn Around Time: Maximum of 40 calendar days, although many tests are completed in 3-4 weeks.

Specimen Requirements: See page 4 of the Requisition Form.

Prices: Sequencing of the *MED12* gene

\$ 1960

CPT Codes:

Sample Ascertainment x1	83890	\$ 30	DNA Isolation x1	83891	\$ 40
Amplification x45	83898	\$ 660	Sequencing x45	83904	\$ 980
Separation x1	83894	\$ 130	Interpretation/Report x1	83912	\$ 120

Accreditation Info. CLIA ID #: 52D1027685 (expires 1/18/13) (CAP#: 7185561, AU ID: 1407125 expires 12/20/12)

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