Marinesco-Sjogren Syndrome: **SIL1 Gene Deletion/Duplication**

**Test Code:** DSIL1  
**Turnaround time:** 2 weeks  
**CPT Codes:** 81228 x1

### Condition Description

Marinesco-Sjogren syndrome (MSS) is characterized by cerebellar ataxia with cerebellar atrophy, early-onset (not necessarily congenital) cataracts, mild to severe mental retardation, hypotonia, and muscle weakness. Additional features include short stature, various skeletal abnormalities including scoliosis, hypergonadotropic hypogonadism, dysarthria, strabismus, and nystagmus. Children with MSS usually present with muscular hypotonia in early infancy; distal and proximal muscular weakness is noticed during the first decade of life. Later, cerebellar findings of truncal ataxia, dysdiadochokinesia, and dysarthria become apparent. Motor function worsens progressively for some years, then stabilizes at an unpredictable age and degree of severity. Cataracts can develop rapidly and typically require lens extraction in the first decade of life. Although many adults are severely handicapped, life span in MSS seems to be near normal.

Diagnosis is based on clinical, radiographic, and neuroimaging studies. Serum CK concentrations are normal or moderately increased (usually 2-4 times the upper normal limits). Light microscopy shows variation in muscle fiber size, atrophic fibers, fatty replacement, and rimmed vacuole formation. Electron microscopy reveals autophagic vacuoles, membranous whorls, and electron-dense double-membrane structures associated with nuclei, which are thought to be a specific ultrastructural feature of MSS. **SIL1** (5q31) is the only gene known to be associated with Marinesco-Sjogren syndrome and mutations in **SIL1** are identified in 50-60% of individuals fulfilling diagnostic criteria.

MSS is inherited in an autosomal recessive manner. MSS has previously been called Garland-Moorhouse syndrome, Marinesco-Garland syndrome, and hereditary oligophrenic cerebello-lental degeneration. MSS is panethnic; the prevalence is not known, but the carrier frequency in Finland is estimated to be approximately 1 in 96.

For patients with suspected Marinesco-Sjogren syndrome, 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:

### Genes

**SIL1**

### Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of Marinesco-Sjogren syndrome in individuals who have tested negative for sequence analysis
- Carrier testing in adults with a family history of Marinesco-Sjogren syndrome who have tested negative for sequence analysis

### 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.

Please note that a “backbone” of probes across the entire genome are included on the array for analytical and quality control purposes. Rarely, off-target copy number variants causative of disease may be identified that may or may not be related to the patient’s phenotype. Only known pathogenic off-target copy number variants will be reported. Off-target copy number variants of unknown clinical significance will not be reported.

### 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

* 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

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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

- Sequence analysis of the *SIL1* gene is available and is required before deletion/duplication analysis.
- Prenatal testing is available to couples who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.