Smith-Magenis Syndrome: RAI1 Gene Deletion/Duplication

**Test Code:** DRAI1  
**Turnaround time:** 2 weeks  
**CPT Codes:** 81228 x1

**Condition Description**

Smith-Magenis syndrome (SMS) is characterized by behavioral abnormalities, including the “self-hug” and “lick and flip” behaviors, significant sleep disturbances, and self-injurious behaviors; distinctive facial features that progress with age, mild to moderate intellectual disability, and developmental delay. Additionally, individuals with SMS have mild to moderate infantile hypotonia with feeding difficulties and failure to thrive, minor skeletal anomalies, short stature, eye abnormalities, otolaryngologic abnormalities, early speech delays with or without hearing loss, and peripheral neuropathy. SMS is caused by deletions or mutations of the *RAI1* (17p11.2) gene.

For patients with suspected SMS, deletion/duplication analysis is recommended as the first step in mutation identification. For patients in whom mutations are not identified by deletion/duplication analysis, full gene sequencing is appropriate.

**References:**
- GeneReviews  
- OMIM #607642: RAI1 gene  
- OMIM #182290: SMS

Deletion/Duplication testing should be ordered as the first tier test.

**Genes**

*RAI1*

**Indications**

This test is indicated for:
- Confirmation of a clinical diagnosis of Smith-Magenis syndrome.
- Carrier testing in adults with a family history of Smith-Magenis syndrome.

**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**

~90% are detected by deletion/duplication analysis. 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) 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.

**Related Tests**

- Sequence analysis of the *RAI1* gene is available for those individuals in whom deletion/duplication 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.