Rigid Spine with Muscular Dystrophy Type 1 (RSMD1): **SELENON** Gene Sequencing

<table>
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<tr>
<th>Test Code: SSEP1</th>
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<td>Turnaround time: 4 weeks</td>
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<td>CPT Codes: 81479 x1</td>
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**Condition Description**

The congenital muscular dystrophies are a group of genetically and clinically heterogeneous hereditary myopathies characterized by congenital hypotonia and muscle weakness, contractures, and delayed motor development. Muscle biopsy usually reveals a nonspecific dystrophic pattern. The clinical course is broadly variable and can involve the brain and eyes. Initial testing often includes clinical evaluation, muscle imaging, electromyography, and muscle biopsy, followed by targeted genetic testing.

Rigid spine with muscular dystrophy type 1 (RSMD1) is an autosomal recessive condition characterized by hypotonia, neck weakness, early scoliosis, muscle weakness, and respiratory insufficiency. The first symptoms are usually hypotonia and poor head control in the neonatal period. Rigidity of the spine evolves into scoliosis. Other features include proximal weakness of the limbs which can lead to a waddling gait and Gowers' sign, mild contractures of the extremities, and respiratory failure that can require nocturnal ventilatory assistance. Age of onset is approximately birth to one year of age; some individuals learn to walk around two and a half years of age while others never walk. A broad phenotypic spectrum has been observed.

Serum creatine kinase (CK) levels are normal to mildly elevated, and immunohistochemistry of muscle tissue shows normal laminin alpha 2 (mersoin) staining. Mutations in the **SELENON** gene (1p36-p35) cause RSMD1. **SELENON** mutations also cause mutliminicore disease and desmin-related myopathy with Mallory body-like inclusions.

For patients with suspected RSMD1, 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**

**SELENON**

**Indications**

This test is indicated for:

- Confirmation of a clinical diagnosis of RSMD1
- Carrier testing in adults with a family history of RSMD1

**Methodology**

PCR amplification of 13 exons contained in the **SELENON** gene as well as the SECIS region of the 3'UTR is performed on the patient's genomic DNA. Direct sequencing of amplification products is performed in both forward and reverse directions, using automated fluorescence dideoxy sequencing methods. The patient's gene sequences are then compared to a normal reference sequence. Sequence variations are classified as mutations, benign variants unrelated to disease, or variations of unknown clinical significance. Variants of unknown clinical significance may require further studies of the patient and/or family members. This assay does not interrogate the promoter region, deep intronic regions, or other regulatory elements, and does not detect large deletions.

**Detection**

Clinical 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 biochemical phenotype.

Analytical Sensitivity: ~99%

**Specimen Requirements**

*Submit only 1 of the following specimen types*

**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 72 hours of collection. Do not freeze.

**Type: DNA, Isolated**

**Specimen Requirements:**
Microtainer
8µg
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: Saliva**

**Specimen Requirements:**
Oragene™ Saliva Collection Kit
Orangene™ Saliva Collection Kit used according to manufacturer instructions. Please contact EGL for a Saliva Collection Kit for patients that cannot provide a blood sample.

Specimen Collection and Shipping:
Please do not refrigerate or freeze saliva sample. Please store and ship at room temperature.

**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 EGL Genetics, please submit a copy of the sequencing report with the test requisition.

**Related Tests**
- Deletion/duplication analysis of the SELENON gene by CGH array is available for those individuals in whom sequence analysis is negative.
- Familial mutation testing is available to family members if mutations are identified by targeted mutation testing or sequencing 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.