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

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 multimicrocore 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

- Preferred specimen type: Whole Blood

Type: Whole Blood

Specimen Requirements:

In EDTA (purple top) or ACD (yellow top) tube:
Infants (Children (>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**

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**

- 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.