Rigid Spine with Muscular Dystrophy Type 1 (RSMD1): \textit{SELENON} Gene Deletion/Duplication

\textbf{Test Code:} DSEP1  
\textbf{Turnaround time:} 2 weeks  
\textbf{CPT Codes:} 81228 x1

\textbf{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 \textit{SELENON} gene (1p36-p35) cause RSMD1. \textit{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.

\textbf{References}


\textbf{Genes}

\textit{SELENON}

\textbf{Indications}

This test is indicated for:

- Confirmation of a clinical diagnosis of RSMD1 in an individual in whom sequence analysis was negative
- Carrier testing in adults with a family history of RSMD1 in whom sequence analysis was negative

\textbf{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.

\textbf{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.

\textbf{Specimen Requirements}

Submit only 1 of the following specimen types

* Preferred specimen type: Whole Blood

\textbf{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

Disclaimer: This information is confidential and subject to change without notice. It may not be reproduced in whole or part unless authorized in writing by an authorized EGL representative.
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 EGL Genetics, please submit a copy of the sequencing report with the test requisition.

**Related Tests**

- Sequence analysis of the **SELENON** 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.