

## Distal Myopathy 2 via *MATR3* Sequence Analysis (Test 336)

**Brief Description of Clinical Features:** A mutation in the matrin 3 protein, encoded by *MATR3* (OMIM #164015), has been found to be causative for a form of distal myopathy often associated with vocal cord and pharyngeal weakness (VCPDM; OMIM #606070). Two large families, one of North American origin (Feit et al. *Am J Hum Genet* 63:1732-1742, 1998) and one of Bulgarian origin (Senderek et al. *Am J Hum Genet* 84:511-518, 2009) demonstrate autosomal dominant inheritance of a distal myopathy with onset typically between 35-57 years of age. The earliest sign among patients from these families is usually ankle and feet muscle weakness, although some cases present with hand weakness and in still others the first symptom is voice change. The pattern of weakness of the hands is unique because the extensors are each affected to varying degrees (Feit et al. 1998). An asymmetric pattern of muscle involvement is typical in the early stage of the disease but slow progression leads to symmetric weakness of the distal muscles. Shoulder and pelvic girdle muscles are eventually affected but ambulation is preserved. Most affected individuals have some vocal cord or swallowing complications. Muscle biopsies from affected individuals reveal variation in fiber size, fiber splitting, and rimmed vacuoles (Senderek et al. 2009). Serum CK levels are at the most only moderately elevated.

**Genetics:** Distal myopathy with vocal cord and pharyngeal weakness associated with a *MATR3* mutation is inherited as an autosomal dominant condition. The same exon 2 p.Ser85Cys mutation has been found on two distinct haplotype backgrounds in two VCPDM families indicating at least two unique mutational origins (Senderek et al. 2009). No other *MATR3* mutations have been reported. Matrin 3 is expressed in skeletal muscle and is a nuclear matrix protein.

**Description of This Particular Test:** Matrin 3 is encoded by exons 2 – 15 of the *MATR3* gene at chromosome 5q31. Testing is accomplished by amplifying each coding exon and ~50 bp of adjacent noncoding sequence, then determining the nucleotide sequence using standard dideoxy sequencing methods and a capillary electrophoresis instrument. Testing for the p.Ser85Cys mutation may be requested separately.

**Reference Sequences:**                      **Genomic:** NC\_000005.8                      **CCDS 4210.1**

**Indication for Testing:** Individuals with distal myopathy and vocal cord and pharyngeal weakness with autosomal dominant inheritance.

**Sensitivity of test:** Analytical sensitivity for the known missense mutation is expected to be close to 100%. Clinical sensitivity cannot be estimated at this time.

**Turn Around Time:** Maximum of 40 days, although many tests are completed in 2-3 weeks.

**Specimen Requirements:** See page 4 of the Requisition Form.

**Price:**                      **Sequencing of *MATR3*:**                      **Exon 2 (test #100): \$ 190**                      **Exons 2 – 15 (test #336): \$ 820**

**CPT Codes:**

Sample Ascertainment x1	83890	\$ 30	DNA Isolation x1	83891	\$ 40	
Amplification x	14	83898	\$ 250	Sequencing x14	83904	\$ 370
Separation x1		83894	\$ 50	Interpretation/Report x1	83912	\$ 80

**Accreditation Info.** CLIA ID #: 52D1027685 (expires 1/18/13) (CAP#: 7185561, AU ID: 1407125 expires 12/20/12)

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