

**Merosin-Deficient Congenital Muscular Dystrophy (MDC1A)  
 via *LAMA2* Gene Sequencing (Test # 345)  
 (Test # 245, Mexican Exon 55 Mutation)**

**Brief Description of Clinical Features:** Merosin-deficient congenital muscular dystrophy (MDC1A; OMIM 607855) is characterized clinically by muscle weakness, delayed motor milestones, white matter changes, mental retardation, hypotonia and seizures (Philpot et al. *Neuromusc Disord* 9:81-85, 1999). However, notable variation in phenotypic severity, age of onset and disease progression has been reported (Jones et al. *J Med Genet* 38: 649-657, 2001). Muscle histology includes dystrophic features and adipose infiltration, but other findings typical of Duchenne biopsies are less apparent (Taniguchi et al. *Biochem Biophys Res Commun* 342: 489-502, 2006).

**Genetics:** The *LAMA2* gene codes for the  $\alpha$ -2 subunit of LAMININ-2 (merosin), the main laminin of muscle tissue. MDC1A is inherited as an autosomal recessive disorder. Mutations are distributed throughout the coding region and some genotype-phenotype correlations have been made (<http://www.dmd.nl/>; Muntoni and Voit, *Neuromuscul Disord* 14:635-49, 2004). An exon 55 nonsense mutation (c.7732C>T; p.Arg2578Stop) has been found by us and others (Coral-Vazquez et al. *J Hum Genet* 48:91-95, 2003) as a recurring cause of MDC1A in individuals with Mexican ancestry.

**Description of This Particular Test:** The  $\alpha$ -2 subunit of LAMININ-2 is coded by exons 1-65 of the *LAMA2* gene located on chromosome 6q22-q23. Testing is accomplished by amplifying all the coding exons and ~50 bp of adjacent noncoding sequence, then determining the nucleotide sequence using standard dideoxy sequencing methods and capillary electrophoresis. Patients of Mexican origin can be tested for the exon 55 mutation prior to full gene sequencing.

**Reference Sequences:** Genomic: NC\_000006.10 mRNA: NM\_000426.2 Protein: NP\_000417.2

**Indication for Testing:** Individuals with symptoms consistent with CMD. Individuals with immunofluorescence results demonstrating complete merosin deficiency.

**Sensitivity of Test:** Merosin-deficient CMD is thought to account for ~50% of all CMD. Because CMD demonstrates extensive locus and allelic heterogeneity, a negative *LAMA2* sequence result does not rule out a diagnosis of this disorder when classic clinical findings are present. If a muscle biopsy is available, immunostaining may also be an appropriate diagnostic approach. Most patients with partial merosin deficiency do not have *LAMA2* mutations (Tezak et al., *Hum Mutat* 21:103-11, 2003). In these cases, evaluation of other CMD genes may be a reasonable diagnostic approach.

**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 *LAMA2* Exon 55 only (Test #245): \$ 190 Exons 1-65 (Test #345): \$ 2990

**CPT Codes:**

Sample Ascertainment	83890	\$ 30	DNA Isolation	83891	\$ 40
Amplification x64	83898	\$1080	Sequencing x64	83904	\$1620
Separation	83894	\$ 80	Interpretation/Report	83912	\$ 140

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

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