

Autosomal Recessive Limb Girdle Muscular Dystrophy Panel - (Test #360)

Brief Description of Clinical Features: Limb girdle muscular dystrophy (LGMD) is a descriptive term for a group of disorders with atrophy and weakness of proximal girdle muscles and typical sparing of the heart and bulbar muscles. Clinical severity, age of onset, and disease progression are highly variable among the subtypes (Sáenz et al. *Brain* 128:732-742, 2005). Serum creatine kinase levels are typically elevated, and muscle biopsies demonstrate a dystrophic process.

Genetics: Autosomal recessive limb girdle muscular dystrophy (LGMD2) is more common than dominantly inheritance LGMD. If a muscle biopsy is available, immunostaining may also be a useful diagnostic approach to help focus molecular testing.

Description of This Particular Test: The following genes are tested in the order specified by the client. Testing is accomplished by amplifying the coding exons and ~50 bp of adjacent noncoding sequence, then determining the nucleotide sequence using standard dideoxy sequencing methods and a capillary electrophoresis instrument.

Reference Sequences:

Gene:	Subtype:	Genomic: NC_	mRNA: NM_	Protein: NP_	CCDS:
<i>CAPN3</i>	LGMD2A	000015.8	000070.2	000061.1	45245.1
<i>DYSF</i>	LGMD2B	000002.10	001130978.1	001124450.1	46326.1
<i>SGCG</i>	LGMD2C	000013.10	000231.2	000222.1	9299.1
<i>SGCA</i>	LGMD2D	000017.9	000023.1	000014.1	32679.1
<i>SGCB</i>	LGMD2E	000004.10	000232.3	000223.1	3488.1
<i>SGCD</i>	LGMD2F	000007.13	003919.2	003910.1	5637.1
<i>TCAP</i>	LGMD2G	000017.9	003673.3	003664.1	11342.1
<i>TRIM32</i>	LGMD2H	000009.11	012210.3	036342.2	6817.1
<i>FKRP</i>	LGMD2I	000019.8	001039885.1	001034974.1	12691.1
<i>TTN</i> (exons 307-312)	LGMD2J	000002.11	133378.3	596869.4	not available
<i>TMEM16E</i> (<i>ANO5</i>)	LGMD2L	000011.8	213599.2	998764.1	31444.1

Indication for Testing: Individuals with clinical symptoms consistent with LGMD and autosomal recessive inheritance. Initial clinical signs are often tiptoe walking, difficulty in running, and scapular winging. Individuals with immunofluorescence results demonstrating absent or reduced staining of the corresponding protein in muscle tissue.

Sensitivity of Test: Many of the LGMD2 subtypes are ultra-rare disorders and clinical sensitivity cannot be estimated. In a large cohort of North American LGMD patients Moore et al. (*J Neuropathol Exp Neurol* 65:995-1003) made a diagnosis of dysferlinopathy in 18% of the cohort using a combined immuno and molecular approach, making *DYSF* the most common cause of LGMD in this mixed population. Childhood onset LGMD is more likely to be caused by defects in the sarcoglycans (Vainzof et al. *J Neurol Sci* 164:44-49, 1999).

Turnaround Time: Approximately 2 to 3 weeks per gene or maximum of 80 days for the panel.

Specimen Requirements: See page 4 of the Requisition Form.

Price: Sequencing of *CAPN3*, *DYSF*, *SGCG*, *SGCA*, *SGCB*, *SGCD*, *TCAP*, *TRIM32*, *FKRP*, *TTN*, *TMEM16E* Genes:

CPT	<i>CAPN3</i>	<i>DYSF</i>	<i>SGCG</i>	<i>SGCA</i>	<i>SGCB</i>	<i>SGCD</i>	<i>TCAP</i>	<i>TRIM32</i>	<i>FKRP</i>	<i>TTN</i>	<i>TMEM16E</i>	Panel
83890	\$30 x1	\$30 x1	\$30 x1	\$30 x1	\$30 x1	\$30 x1	\$30 x1	\$30 x1	\$30 x1	\$30 x1	\$30 x1	\$30 x1
83891	\$40 x1	\$40 x1	\$40 x1	\$40 x1	\$40 x1	\$40 x1	\$40 x1	\$40 x1	\$40 x1	\$40 x1	\$40 x1	\$40 x1
83898	\$335 x21	\$ 850 x51	\$150 x7	\$130 x8	\$110 x6	\$160 x11	\$90 x3	\$120 x6	\$90 x3	\$410 x26	\$320 x21	\$2,930 x163
83904	\$505 x21	\$1270x51	\$230 x7	\$190 x8	\$160 x6	\$220 x11	\$130 x3	\$170 x6	\$140 x3	\$610 x26	\$490 x21	\$4,390 x163
83894	\$70 x1	\$170 x1	\$40 x1	\$30 x1	\$30 x1	\$60 x1	\$30 x1	\$40 x1	\$30x1	\$90 x1	\$90 x1	\$190 x1
83912	\$110 x1	\$130 x1	\$80 x1	\$70 x1	\$70 x1	\$80 x1	\$70 x1	\$90 x1	\$60 x1	\$110 x1	\$120 x1	\$340 x1
Totals:	\$1,090	\$2,490	\$570	\$490	\$440	\$590	\$390	\$ 490	\$390	\$1,290	\$1,090	\$7,920*

*When 6 or more genes on this panel are sequentially tested, a 15% discount will apply to the total cost.

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

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