

**Glycogen Storage Disease, Type V (McArdle Disease) via PYGM Gene Sequencing  
 Sequential (Standard) Test – Test #226; Tier 1 Only - #227; Tier 2 Only - #228**

**Brief Description of Clinical Features:** Glycogen Storage Disease Type V (GSDV) (OMIM 232600), also known as McArdle Disease, is characterized by exercise-induced muscle fatigue, pain and cramps. Onset is usually in the second to third decade. Intense exercise can lead to rhabdomyolysis with concomitant myoglobinuria and renal failure. Patients have elevated serum creatine kinase activity. Severity is highly variable. For more information see [www.agsdus.org](http://www.agsdus.org) and Arenas et al. GeneReviews 2009 (<http://www.geneclinics.org/>).

**Genetics:** GSDV is an autosomal recessive disorder. Defects in the *PYGM* gene encoding the muscle phosphorylase enzyme are the only known cause of GSDV. Roughly 65 different causative mutations have been reported in *PYGM* ([www.hgmd.org](http://www.hgmd.org); Martin et al. Ann Neurol 50:574-581, 2001; Bruno et al. Hum Mut 27:718, 2006). The mutations are missense, nonsense, splicing and frameshift and are located throughout the length of this compact gene. Two mutations: Arg50Stop in exon 1 and Gly205Ser in exon 5 are common among European patients. No genotype-phenotype connections have yet been made. Amino acid numbering differs among research groups; for example Arg50Stop is sometimes referred to as Arg49Stop. A few authors have reported muscle symptoms in carriers of *PYGM* mutations (see for example Manfredi et al. J Neurol Sci 115:91-94, 1993, but see also Andersen et al. Neurol 67:716-718, 2006). Recently, Vladutiu et al. (Muscle Nerve 34:153-162, 2006) reported that among patients with adverse muscle side effects to statins there is a much higher frequency of *PYGM* mutation carriers than among control groups.

**Description of This Particular Test:** This test involves bidirectional sequencing of the coding regions of all 20 *PYGM* exons plus about 50 bp of non-coding flanking DNA on each side. Because of the two common mutations and because the test will sometimes be performed to identify carriers, the test has two tiers. Tier 1 involves sequencing of exons 1 and 5. If two likely causative mutations are detected in patients in Tier 1 or one mutation in carriers in Tier 1, then testing stops. Otherwise, testing continues with Tier 2 involving sequencing of the remaining 18 exons.

**Reference Sequences:** Genomic: NC\_000011.8 mRNA: NM\_005609.1 protein: NP\_005600.1

**Indications for Test:** All patients with symptoms consistent with GSDV are candidates for this test. We will sequence DNA from likely carriers (for example parents of patients). We will sequence one or two, specified exons in members of families with known mutations and in research subjects to confirm research results.

**Sensitivity of Test:** Two causative mutations will apparently be identified in nearly all patients with absence of muscle phosphorylase activity (Martin et al. 2001). The sensitivity in patients who have not had a test for enzyme activity is unknown.

**Turn Around Time:** Maximum of 40 days.

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

**Prices:**

**Tier 1: Sequencing of *PYGM* exons 1 and 5** **\$340**  
**If positive, stop; if negative, then:**  
**Tier 2: Sequencing of the remaining 18 *PYGM* exons** **an additional \$650** **for a total of \$990**  
**Tier 2 alone is \$790**

**CPT Codes:**

Codes	Description	Tier 1 Only	Tier 2 Only	Tier 1 + Tier 2
83890	Ascertainment	\$ 30 (x1)	\$ 30 (x1)	\$ 30 (x1)
83891	DNA Isolation	\$ 40 (x1)	\$ 40 (x1)	\$ 40 (x1)
83898	Amplification	\$ 68 (x2)	\$224 (x12)	\$300 (x14)
83904	Mutation Ident by Sequencing	\$102 (x2)	\$336 (x12)	\$460 (x14)
83894	Separation	\$ 30 (x1)	\$ 60 (x1)	\$ 60 (x1)
83912	Interpretation and Report	\$ 70 (x1)	\$100 (x1)	\$100 (x1)
<b>Totals:</b>		<b>\$340</b>	<b>\$790</b>	<b>\$990</b>

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

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