PREVENTION GENETICS
DISEASE PREVENTION THROUGH GENETIC TESTING

CLIA #: 52D1027685 ● CAP #: 7185561
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Glycogen Storage Disease Type III via *AGL* Gene Sequencing (Test #224)

Brief Description: Glycogen Storage Disease Type III (GSDIII) (OMIM 232400) is caused by a deficiency of glycogen debranching enzyme. Symptoms, which appear in the first year of life, include hepatomegaly, fasting hypoglycemia, short stature, and often myopathy (muscle wasting) and/or hypertrophic cardiomyopathy. Symptoms are quite variable among affected individuals. Symptoms are also similar to GSD Type I. Several subtypes of GDSIII have been described based on phenotypic differences, but so far all subtypes have been connected to deficiencies in the same debranching enzyme. For further information see http://www.agsdus.org/.

Genetics: GSDIII is inherited in an autosomal recessive manner. All causative genetic defects reported to date for GDSIII have been within the large *AGL* gene encoding the glycogen debranching enzyme with both transferase and glucosidase activities. Approximately 75 different mutations have been identified in *AGL* (see for example Shen et al. J Clin Invest 98:352-357, 1996; Okubo et al. Hum Genet 106:108-115, 2000; Lucchiari et al. Amer J Med Genet 109:183-190, 2002; Endo et al J Hum Genet 51:958-963, 2006; Human Gene Mutation Database (http://www.hgmd.org/)). The mutations are distributed throughout the length of the gene. Causative mutations are largely nonsense, splicing, and frameshift, with a few missense. No mutations are predominant, except in isolated populations.

Description of This Particular Test: This test involves DNA sequencing of all 33 coding exons of the predominant isoform of *AGL* (yielding a protein with 1532 amino acids) plus about 50 bp of flanking non-coding DNA on each side.

Indications for Test: Candidates for this test are patients with symptoms consistent with GSDIII. We will sequence the *AGL* gene in parents of affected children in cases where DNA from the child(ren) is unavailable. We will also perform sequencing of any single exon or pair of exons for family members of patients with known mutations and to confirm research results ($190-340 charge).

Sensitivity of Test: Based on literature reports, we estimate that our full gene sequencing test will detect at least one likely causative mutation in nearly all patients with GSDIII. In 6/20 cases (30%) reported in the literature, only one of the two mutations was detected.

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.

Prices: **Sequencing of the *AGL* gene** **$1790**

CPT Codes:

Sample Ascertainment	83890	$ 30	DNA Isolation	83891	$ 40
Amplification x28	83898	$ 590	Sequencing x28	83904	$ 870
Separation	83894	$ 110	Interpretation/Report	83912	$ 150

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

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