Glycogen Storage Disease V (McArdle Disease): PYGM Gene Deletion/Duplication

**Condition Description**

Myophosphorylase deficiency (or McArdle disease) is an autosomal recessive disorder caused by mutations in the myophosphorylase gene (PYGM) located on chromosome 11 (11q13). Patients experience exercise intolerance with premature fatigue, myalgias, and cramps that are exacerbated by exercise. A second wind phenomenon is described in many patients and is characterized by an improved exercise tolerance after a brief reduction in the intensity of exercise or a brief rest. This response is mediated by an adaption to the substrate-limited oxidative phosphorylation by increased mobilization and delivery of free fatty acids to muscle as an energy source, increased blood flow, and increased glucose oxidation. About half of patients experience exercise intolerance with muscle necrosis and myoglobinuria after exercise. This rhabdomyolysis can produce acute renal failure.

Muscle weakness is present in approximately 33% of patients. The onset of exercise intolerance is often observed in childhood, but clinical ascertainment is usually in the second or third decade. Atypical variants of the disease may occur and be confined to complaints of easy fatigability without cramps or myoglobinuria. In some individuals, weakness may not be apparent until the seventh or eighth decade of life.

Serum creatine kinase is elevated in over 90% of patients with myophosphorylase deficiency. Forearm ischemic exercise testing produces essentially no increase in venous lactate. Muscle pathology often shows subsarcolemmal and intermyofibrillar vacuoles filled with glycogen. Histochemical staining for myophosphorylase activity is absent.

Three point mutations (R49X, G204S, and K542T) account for 71% of the McArdle disease alleles. For patients in whom only one or no mutations are identified through target testing, full sequence analysis can be used to detect the other mutation(s).

Please [click here](https://eglgenetics.com) for the GeneReviews summary on this condition.

**Genes**

PYGM

**Indications**

This test is indicated for:

- Confirmation of a clinical diagnosis of myophosphorylase deficiency in individuals who have tested negative for sequence analysis
- Carrier testing in adults with a family history of myophosphorylase deficiency who have tested negative for sequence analysis

**Methodology**

DNA isolated from peripheral blood is hybridized to a CGH array to detect deletions and duplications. The targeted CGH array has overlapping probes which cover the entire genomic region.

Please note that a “backbone” of probes across the entire genome are included on the array for analytical and quality control purposes. Rarely, off-target copy number variants causative of disease may be identified that may or may not be related to the patient’s phenotype. Only known pathogenic off-target copy number variants will be reported. Off-target copy number variants of unknown clinical significance will not be reported.

**Detection**

Detection is limited to duplications and deletions. The CGH array will not detect point or intronic mutations. Results of molecular analysis must be interpreted in the context of the patient's clinical and/or biochemical phenotype.

**Specimen Requirements**

Submit only 1 of the following specimen types

* Preferred specimen type: Whole Blood

**Type: Whole Blood**

Specimen Requirements:

In EDTA (purple top) or ACD (yellow top) tube:
- Infants (2 years): 3-5 ml
- Older Children & Adults: 5-10 ml

Specimen Collection and Shipping: Refrigerate until time of shipment. Ship sample within 5 days of collection at room temperature with overnight delivery.

**Type: Saliva**
Specimen Requirements:

Oragene™ Saliva Collection kit (available through EGL) used according to manufacturer instructions.

Specimen Collection and Shipping: Store sample at room temperature. Ship sample within 5 days of collection at room temperature with overnight delivery.

Special Instructions

Submit copies of diagnostic biochemical test results with the sample, if appropriate. Contact the laboratory if further information is needed.

Sequence analysis is required before deletion/duplication analysis by targeted CGH array. If sequencing is performed outside of Emory Genetics Laboratory, please submit a copy of the sequencing report with the test requisition.

Related Tests

- Sequence analysis of the PYGM gene is available and is required before deletion/duplication analysis.
- Prenatal testing is available to couples who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.