## Condition Description

Phosphoglycerate kinase-1 (PGK) deficiency is an X-linked condition with a highly variable clinical phenotype that can include hemolytic anemia, myopathy, rhabdomyolysis, intellectual disability, and other neurologic involvement. These symptoms may occur individually or in various combinations. The anemia may be severe and transfusion dependent. Episodes of rhabdomyolysis, myoglobinuria, and acute renal failure may occur without hemolytic anemia, especially after exercise. Reported neurological manifestations include seizures, severe encephalopathy, spastic tetraparesis, and hemiplegic migraines.

Individuals with PGK deficiency tend to fall into two groups: those that have a predominantly hemolytic form and those that have a predominantly myopathic form. Varying degrees of intellectual disability and other neurological symptoms can be seen in both forms. The clinical phenotype is usually similar in affected individuals in the same family. Female carriers of PGK deficiency may show chronic, mild hemolytic anemia.

Mutations in the **PGK1** gene (Xq13) cause PGK deficiency. Most families have unique mutations. The **PGK1** gene encodes the phosphoglycerate kinase-1 protein, which catalyzes the reversible conversion of 1,3-diphosphoglycerate to 3-phosphoglycerate during glycolysis, generating one molecule of ATP.

For patients with suspected PGK deficiency, sequence analysis is recommended as the first step in mutation identification. For patients in whom mutations are not identified by full gene sequencing, deletion/duplication analysis is appropriate.

### References:
- OMIM #300653: Phosphoglycerate Kinase 1 Deficiency

## Genes

**PGK1**

### Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of PGK.
- Carrier testing in adult females with a family history of PGK.

### Methodology

PCR amplification of 11 exons contained in the **PGK1** gene is performed on the patient's genomic DNA. Direct sequencing of amplification products is performed in both forward and reverse directions, using automated fluorescence dideoxy sequencing methods. The patient's gene sequences are then compared to a normal reference sequence. Sequence variations are classified as mutations, benign variants unrelated to disease, or variations of unknown clinical significance. Variants of unknown clinical significance may require further studies of the patient and/or family members. This assay does not interrogate the promoter region, deep intronic regions, or other regulatory elements, and does not detect large deletions.

### Detection

Clinical Sensitivity: Unknown. Mutations in the promoter region, some mutations in the introns and other regulatory element mutations cannot be detected by this analysis. Large deletions will not be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's biochemical phenotype.

Analytical Sensitivity: ~99%

### 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

- Deletion/duplication analysis of the PGK1 gene by CGH array is available for those individuals in whom sequence analysis is negative.
- A next generation sequence analysis panel of 90+ XLID genes is available.
- A CGH array-based test for deletion/duplication analysis of 90+ XLID genes is available.
- Custom diagnostic mutation analysis (KM) is available to family members if mutations are identified by targeted mutation testing or sequencing analysis.
- Prenatal testing is available only for known familial mutations to individuals who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.