

Glucose-6-Phosphate Dehydrogenase (G6PD) Deficiency: *G6PD* Gene Sequencing

Test Code: JS

Turnaround time: 4 weeks

CPT Codes: 81479 x1

Condition Description

Glucose-6-Phosphate Dehydrogenase (G6PD) deficiency is the most common human enzyme deficiency; an estimated 400 million people worldwide are affected [1]. G6PD deficiency is an X-linked condition that causes destruction of red blood cells. G6PD is in the hexose monophosphate pathway, the only NADPH-generation process in mature red blood cells, which lack the citric acid cycle. Deficiency of G6PD, in various forms, is the basis of favism, primaquine sensitivity and some other drug-sensitive hemolytic anemias, anemia and jaundice in the newborn, and chronic hemolytic anemia. Symptoms of a hemolytic crisis can include dark urine, an enlarged spleen, fatigue, paleness, shortness of breath, rapid heart rate, and jaundice. Severe hemolytic crisis can produce hemoglobinuria. Laboratory tests may reveal an elevated absolute reticulocyte count, elevated bilirubin levels, elevated serum LDH, low red blood cell count, and low hemoglobin levels. Transfusions may occasionally be needed. Spontaneous recovery from hemolytic crises is the usual outcome, although kidney failure or death may occur following a severe hemolytic event.

Different variants of the enzyme are found in high frequency in African, Mediterranean, and Asiatic populations [2]. Heterozygote advantage from malaria has been proposed to account for the high frequency of the particular alleles in particular populations [3]. The G6PD (Xq28) variants have been divided into 5 classes according to the level of enzyme activity. These are: class 1--enzyme deficiency with chronic hemolytic anemia; class 2--severe enzyme deficiency (less than 10%); class 3--moderate to mild enzyme deficiency (10-60%); class 4--very mild or no enzyme deficiency (60%); class 5--increased enzyme activity.

References:

1. Scriver et al. "Glucose-6-Phosphate Dehydrogenase Deficiency." In: The metabolic and molecular bases of inherited disease. 1995. 7th ed. n.p.: McGraw- Hill, Inc.:3367-98.
2. Porter et al. Variation of glucose-6-phosphate dehydrogenase in different populations. Lancet 1964, 1:895-899.
3. Luzzatto et al. Glucose-6-phosphate dehydrogenase deficient red cells: resistance to infection by malarial parasites. Science 1969, 164:839-842.
4. Noori-Dalooi et al. A comprehensive study on the major mutations in glucose-6-phosphate dehydrogenase-deficient polymorphic variants identified in the coastal provinces of Caspian Sea in the north of Iran. Clin. Biochem. 2007, 40:699-704.
5. Laosombat et al. Molecular heterogeneity of glucose-6-phosphate dehydrogenase (G6PD) variants in the south of Thailand and identification of a novel variant (G6PD Songklanagarind). Blood Cells Mol. Dis. 2005, 34:191-196.

Genes

[G6PD](#)

Indications

This test is indicated for:

- Confirmation of a clinical/biochemical diagnosis of G6PD deficiency
- Carrier testing in females/adults with a family history of G6PD deficiency

Methodology

PCR amplification of 12 protein-encoding exons contained in the *G6PD* gene is performed on patient genomic DNA. Direct sequencing of amplification products is performed in both the forward and reverse directions using automated fluorescence dideoxy sequencing methods. Patient gene sequences are compared to a normal reference sequence. Sequence variations are then 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. Large deletions are not detected by this analysis.

Detection

Clinical Sensitivity: 241/248 mutations identified in Iranian patients with a history of favism [4], 134/134 nucleotide changes (122 known mutations and 12 uncharacterized variants) identified in G6PD deficient patients in Thailand [5].

Analytical Sensitivity: ~99%

Specimen Requirements

Submit only 1 of the following specimen types

Type: DNA, Isolated

Specimen Requirements:

Microtainer

8µg

Isolation using the Perkin Elmer™ Chemagen™ Chemagen™ Automated Extraction method or Qiagen™ Puregene kit for DNA extraction is recommended.

Specimen Collection and Shipping:

Refrigerate until time of shipment in 100 ng/μL in TE buffer. Ship sample at room temperature with overnight delivery.

Type: Whole Blood (EDTA)**Specimen Requirements:**

EDTA (Purple Top)

Infants and Young Children (2 years of age to 10 years old: 3-5 ml

Older Children & Adults: 5-10 ml

Autopsy: 2-3 ml unclotted cord or cardiac blood

Specimen Collection and Shipping:

Ship sample at room temperature for receipt at EGL within 24 hours of collection. Do not refrigerate or freeze.

Type: Saliva**Specimen Requirements:**

Oragene™ Saliva Collection Kit

Oragene™ Saliva Collection Kit used according to manufacturer instructions. Please contact EGL for a Saliva Collection Kit for patients that cannot provide a blood sample.

Specimen Collection and Shipping:

Please do not refrigerate or freeze saliva sample. Please store and ship at room temperature.

Special Instructions

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

Related Tests

- Custom Diagnostic Mutation Analysis (KM) is available to family members if mutations are identified by sequencing.
- Prenatal testing is available for known familial mutations only. Please call the Laboratory Genetic Counselor before collecting a fetal sample.