Glucose-6-Phosphate Dehydrogenase (G6PD) Deficiency: \textit{G6PD} Gene Sequencing

\textbf{Test Code:} JS  
\textbf{Turnaround time:} 4 weeks  
\textbf{CPT Codes:} 81479 x1

\section*{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 \textit{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.

\section*{References:}

\section*{Genes}

\textbf{G6PD}

\section*{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

\section*{Methodology}

PCR amplification of 12 protein-encoding exons contained in the \textit{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.

\section*{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: \textasciitilde 99%

\section*{Specimen Requirements}

Submit only 1 of the following specimen types
- Preferred specimen type: Whole Blood

\textbf{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. 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.