Galactosemia (Galactokinase Deficiency): \textit{GALK1} Gene Sequencing

**Test Code:** IQ  
**Turnaround time:** 4 weeks  
**CPT Codes:** 81479 x1

### Condition Description

Galactokinase (GALK) deficiency is one of the three known forms of galactosemia, along with galactose-1-phosphate uridylyltransferase (GALT) deficiency (classic galactosemia) and UDP-galactose-4-epimerase (GALE) deficiency \cite{1-2}. GALK deficiency is an autosomal recessive disorder characterized by an elevation of blood galactose concentration and diminished galactose-1-phosphate concentration, leading to production of alternative metabolic products such as galactitol \cite{3}. Galactokinase-deficiency may present in the neonatal period with cataracts; no other clinical complications have been consistently associated with GALK-deficiency \cite{2}. GALK deficiency should be considered in individuals with cataracts, elevated red cell galactose, galactosuria, or elevated urinary galactitol and normal GALT enzyme activity. GALK activity is used to rule-out variant galactosemia due to galactokinase deficiency which should not be confused with classical galactosemia secondary to GALT deficiency, or epimerase-deficiency galactosemia secondary to GALE deficiency. The vast majority of patients with biochemical diagnosis of GALK deficiency have mutations in the GALK1 \cite{17q25} gene \cite{4-6}. Gene sequence analysis is available to test for mutations in the GALK1 gene in patients with a biochemical diagnosis of GALK deficiency (IQ). For patients with mutations not identified by full gene sequencing, a separate deletion/duplication assay is available using a targeted CGH array (JA).


Click [here](http://www.ThinkGenetic.com) for the GeneReviews summary on this condition. Also, refer to the Comprehensive Galactosemia Panel for a disease overview.

### References:

- Sangiulo \textit{et al.} Biochemical Characterization of Two \textit{GALK1} Mutations in Patients with Galactokinase Deficiency. \textit{Hum Mutat} 2004 Apr;23(4):396-403

### Genes

\textbf{GALK1}

### Indications

This test is indicated for:

- Individuals with elevated blood galactose but with normal GALT and GALE enzyme activities.
- Carrier testing for individuals with a family history of GALK deficiency.

### Methodology

PCR amplification of 8 exons contained in the GALK1 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

The vast majority of patients with clinical and biochemical diagnosis will have an abnormal DNA test.  
Clinical Sensitivity: 26/26 mutations identified in 13 patients \cite{8}, 4/4 mutations identified in 2 patients \cite{9}.  
Analytical Sensitivity: \textasciitilde99%  

Detection is limited to duplications and deletions. Array CGH will not detect point mutations 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) 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. Sequence analysis is required before deletion/duplication analysis by targeted CGH array. If sequencing is performed outside of EGL Genetics, please submit a copy of the sequencing report with the test requisition.

**Related Tests**

- GALT and GALE Gene Sequencing for transferase deficient and epimerase deficient galactosemia
- Comprehensive Galactosemia Panel includes: GALT enzyme activity, isozyme pattern, gal-1-P concentration
- Urine Galactitol Concentration
- Custom Diagnostic Mutation Analysis (KM) is available to family members if mutations are identified by sequencing.
- A Deletion/Duplication Assay is available separately for individuals where mutations are not identified by sequence analysis. Refer to the test requisition or contact the laboratory for more information.
- Prenatal testing is available for known familial mutations only. Please call the Laboratory Genetic Counselor before collecting a fetal sample.