Galactosemia (Galactokinase Deficiency): \textit{GALK1} Gene Deletion/Duplication

\textbf{Test Code:} JA  
\textbf{Turnaround time:} 2 weeks  
\textbf{CPT Codes:} 81228 x1

\section*{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 (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).

Visit \url{www.ThinkGenetic.com} for patient-friendly information on galactosemia. Click \url{here} for the GeneReviews summary on this condition. Also, refer to the Comprehensive Galactosemia Panel for a disease overview.

\section*{References}

4. Sangiuolo et al. Biochemical Characterization of Two GALK1 Mutations in Patients with Galactokinase Deficiency Hum Mutat 2004 Apr;23(4):396-403  
5. Park et al. Molecular and biochemical characterization of the GALK1 gene in Korean patients with galactokinase deficiency. Mol Genet Metab. 2007. 91:234-8  

\section*{Genes}

\textit{GALK1}

\section*{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.

\section*{Methodology}

Detection is limited to duplications and deletions. Array CGH will not detect point mutations or intronic mutations.

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.

\section*{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\% Results of molecular analysis must be interpreted in the context of the patient's clinical and/or biochemical phenotype.

\section*{Specimen Requirements}

Submit only 1 of the following specimen types

* Preferred specimen type: Whole Blood

\section*{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.
- Prenatal testing is available for known familial mutations only. Please call the Laboratory Genetic Counselor before collecting a fetal sample.