Galactosemia (Epimerase): *GALE* Gene Sequencing

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

### Condition Description

UDP-Galactose-4-Epimerase (GALE) deficiency is one of the three known forms of galactosemia, along with galactose-1-phosphate uridyltransferase (GALT) deficiency (classic galactosemia) and galactokinase (GALK) deficiency [1-2]. GALE deficiency has been defined as a continuous disorder with a spectrum of enzyme impairment and corresponding metabolic compromise impacting a variety of tissues in affected individuals [3]. The patients may present with symptoms reminiscent of classic galactosemia and demonstrate severely impaired GALE activity in both RBCs and lymphoblast resulting in accumulation of abnormally high levels of RBC galactose, gal-1P and UDP-gal. GALE deficiency should be considered in individuals with elevated RBC galactose, gal-1-P and UDP-gal but normal GALT enzyme activity. Mutations in the *GALE* gene, located on 1p36, are associated with a biochemical diagnosis of GALE deficiency [3]. Gene sequence analysis is available to test for mutations in the *GALE* gene in patients with a biochemical diagnosis of GALE deficiency (JU). For patients with mutations not identified by full gene sequencing, a separate deletion/duplication assay is available using a targeted CGH array (JV).

**Click here** for the GeneReviews summary on this condition. Also, refer to the Comprehensive Galactosemia Panel for a disease overview.

### References:


### Genes

**GALE**

### Indications

This test is indicated for:  
- Individuals with elevated gal-1-P and UDP-gal but with normal GALT and GALK enzyme activity and biochemical findings consistent with GALE deficiency  
- Carrier testing for individuals with a family history of GALE deficiency

### Methodology

PCR amplification of 10 exons contained in the *GALE* 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

One study identified 23 distinct base changes in 8 patients, of which 20 were novel [3]. 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**

**Type: Saliva**

**Specimen Requirements:**  
Oragene™ Saliva Collection Kit  
Orangene™ 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.

**Type: DNA, Isolated**

**Specimen Requirements:**  
Microtainer  
8µg
Isolation using the Perkin Elmer™ 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

**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. Contact the laboratory if further information is needed.

**Related Tests**
- **Sequencing of GALT and GALK Genes** for transferase deficient and galactokinase deficient galactosemia
- **Comprehensive Galactosemia Panel** includes: GALT enzyme activity, isozyme pattern, gal-1-P concentration, GALT common mutation panel
- **Urine Galactitol Concentration**
- **Custom Diagnostic Mutation Analysis (KM)** is available to family members if mutations are identified by sequencing.
- For comprehensive testing a deletion/duplication assay is available separately. This test is indicated 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 to couples who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.