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 uridylytransferase (*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

* 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

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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. Contact the laboratory if further information is needed.

Click here for the Epimerase Deficiency Clinical Information Form to send with the sample.

**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.