Client: Example Client ABC123
123 Test Drive
Salt Lake City, UT 84108
UNITED STATES

Physician: Doctor, Example

Patient: Patient, Example

DOB	10/7/2024
Gender:	Male
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	00/00/0000 00:00

Galactosemia (GALT) Sequencing and Deletion/Duplication

ARUP test code 3004716

GALT Specimen: Whole Blood

GALT Interp: Negative

RESULT
No pathogenic variants were detected in the GALT gene.

INTERPRETATION
No pathogenic variants were detected in the GALT gene. This result decreases the likelihood of, but does not exclude, a diagnosis of or carrier status for galactosemia 1. Please refer to the background information included in this report for the methodology and limitations of this test.

RECOMMENDATIONS
This result should be correlated with clinical findings and galactose-1-phosphate uridyltransferase (GALT) enzymatic activity. If this individual is of Ashkenazi Jewish ancestry, consideration may be given to additional analysis for the 5 kb deletion via a different methodology, as this assay has reduced analytical sensitivity for this common variant. Genetic consultation is recommended.

COMMENTS
Likely benign and benign variants are not reported.
Variants in the following region(s) may not be detected by NGS with sufficient confidence in this sample due to technical limitations: None

This result has been reviewed and approved by [redacted]

BACKGROUND INFORMATION: Galactosemia (GALT) Sequencing and Deletion/Duplication

CHARACTERISTICS: Galactosemia type 1 is a disorder of galactose metabolism resulting from galactose-1-phosphate uridyltransferase (GALT) deficiency and includes phenotypes of classic galactosemia, clinical variant galactosemia, and benign variant galactosemia. Classic galactosemia and clinical variant galactosemia may be life -threatening and clinical findings can include diarrhea, feeding problems, failure to thrive, hepatocellular damage, bleeding, sepsis, or neonatal death. A lactose-restricted diet is required and typically prevents neonatal complications when initiated in first days of life. Even with adequate early treatment, individuals with classic galactosemia are at increased risk for developmental delays, speech disorders, motor function issues, and females commonly have premature ovarian insufficiency. Individuals with clinical variant galactosemia who have received adequate early treatment

may not be at risk for long-term complications. Benign variant galactosemia, the most common form being Duarte variant galactosemia (also known as D/G galactosemia) is associated with partial deficiency in erythrocyte GALT enzyme, but is typically not associated with clinical disease; thus, dietary therapy is often not recommended.

EPIDEMIOLOGY: Prevalence of classic galactosemia is 1 in 48,000 in the U.S.

CAUSE: Pathogenic biallelic germline variants in the GALT gene.

INHERITANCE: Autosomal recessive.

PENETRANCE: 100 percent for classic or clinical variant galactosemia.

CLINICAL SENSITIVITY: Approximately 95 percent.

GENE TESTED: GALT (NM_000155).

METHODOLOGY: Probe hybridization-based capture of all coding exons and exon-intron junctions of the GALT gene, followed by massively parallel sequencing. Sanger sequencing was performed as necessary to fill in regions of low coverage and to confirm reported variants that do not meet acceptable quality metrics. A proprietary bioinformatic algorithm was used to detect large (single exon-level or larger) deletions or duplications in the GALT gene. Large deletions/duplications were confirmed using an orthogonal exon-level microarray. Human genome build 19 (Hg 19) was used for data analysis.

ANALYTICAL SENSITIVITY/SPECIFICITY: The analytical sensitivity is approximately 99 percent for single nucleotide variants (SNVs) and greater than 93 percent for insertions/duplications/deletions (indels) from 1-10 base pairs in size. Indels greater than 10 base pairs may be detected, but the analytical sensitivity may be reduced. Deletions of two exons or larger are detected with sensitivity greater than 97 percent; single exon deletions are detected with 62 percent sensitivity. Duplications of three exons or larger are detected at greater than 83 percent sensitivity. Specificity is greater than 99.9 percent for all variant classes.

LIMITATIONS: A negative result does not exclude a diagnosis of galactosemia. This test only detects variants within the coding regions and intron-exon boundaries of the GALT gene. Deletions/duplications/insertions of any size may not be detected by massively parallel sequencing. Regulatory region variants and deep intronic variants will not be identified. Diagnostic errors can occur due to rare sequence variations. In some cases, variants may not be identified due to technical limitations caused by the presence of pseudogenes, repetitive, or homologous regions. This test is not intended to detect low-level mosaic or somatic variants, gene conversion events, complex inversions, translocations, mitochondrial DNA (mtDNA) variants, or repeat expansions. Interpretation of this test result may be impacted if this patient has had an allogeneic stem cell transplantation. Noncoding transcripts were not analyzed.

This test was developed and its performance characteristics determined by ARUP Laboratories. It has not been cleared or approved by the U.S. Food and Drug Administration. This test was performed in a CLIA-certified laboratory and is intended for clinical purposes.

Counseling and informed consent are recommended for genetic testing. Consent forms are available online.

H=High, L=Low, *=Abnormal, C=Critical

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
GALT Specimen	24-296-122101	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
GALT Interp	24-296-122101	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00

END OF CHART

H=High, L=Low, *=Abnormal, C=Critical