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

Physician: Doctor, Example

Patient: Patient, Example

DOB	11/1/2023
Gender:	Male
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	00/00/0000 00:00

Biotinidase Deficiency (BTD) Sequencing

ARUP test code 3004424

Biotinidase Deficiency Specimen	Whole Blood
Biotinidase Deficiency Interp	Negative

RESULT
No pathogenic variants were detected in the BTD gene.

INTERPRETATION
No pathogenic variants were detected the BTD gene. This result significantly decreases the likelihood of, but does not exclude, a biotinidase deficiency. Please refer to the background information included in this report for the methodology and limitations of this test.

RECOMMENDATIONS
Medical screening and management should rely on clinical and biochemical findings and family history. If this individual has a family history, determination of a causative familial variant in an affected family member is necessary for optimal interpretation of this negative result. Further testing may be warranted if there is a familial variant that is not detectable by this assay. 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]

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

BACKGROUND INFORMATION: Biotinidase Deficiency (BTD) Sequencing

CHARACTERISTICS: Deficiency in biotinidase enzymatic activity impairs the body's ability to recycle and reuse the vitamin biotin, resulting primarily in neurologic and dermatologic symptoms. Manifestations of profound biotinidase deficiency (BTD) include ataxia, hypotonia, developmental delay, seizures, vision problems, hearing loss, alopecia, metabolic ketolactic acidosis, organic aciduria, and hyperammonemia.

EPIDEMIOLOGY: The incidence of profound and partial biotinidase deficiency is approximately 1:60,000

CAUSE: Pathogenic germline variants in the BTD gene

INHERITANCE: Autosomal recessive

CLINICAL SENSITIVITY: 99 percent

GENE TESTED: BTD (NM_000060)* (NM_001370658)
* - One or more exons are not covered by sequencing for the indicated gene; see limitations section below.

METHODOLOGY: Probe hybridization-based capture of all coding exons and exon-intron junctions of the targeted genes, followed by massively parallel sequencing. Sanger sequencing was performed as necessary to fill in regions of low coverage and confirm reported variants. 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. Specificity is greater than 99.9 percent for all variant classes.

LIMITATIONS: A negative result does not exclude a diagnosis of BTD. This test only detects variants within the coding regions and intron-exon boundaries of the BTD 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) mutations, or repeat expansions. Interpretation of this test result may be impacted if this patient has had an allogeneic stem cell transplantation. Non-coding transcripts were not analyzed.

SNVs and Indels will not be called in the following regions due to technical limitations of the assay:
BTD (NM_000060) exon(s) 1

This test was developed and its performance characteristics determined by ARUP Laboratories. It has not been cleared or approved by the US 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.

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
Biotinidase Deficiency Specimen	24-102-401568	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Biotinidase Deficiency Interp	24-102-401568	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