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

Physician: Doctor, Example

Patient: Patient, Example

DOB	6/9/1972
Gender:	Male
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	00/00/0000 00:00

Peroxisomal Disorder Panel, Sequencing

ARUP test code 3002700

Peroxisomal Disorders Specimen: Whole Blood

Peroxisomal Disorders Interp: Negative

INDICATION FOR TESTING
Hyperoxaluria.

RESULT
No pathogenic variants were detected in any of the genes tested.

INTERPRETATION
According to information provided to ARUP Laboratories, the patient is a 49 year old with hyperoxaluria. No pathogenic variants were identified by massively parallel sequencing of the coding regions and exon-intron boundaries of the genes tested, including AGXT. This result decreases the likelihood of, but does not exclude, a heritable form of peroxisomal dysfunction. Please refer to the background information included in this report for a list of the genes analyzed and limitations of this test.

RECOMMENDATIONS
Medical screening and management should rely on clinical findings and biochemical/functional assays. The only gene examined by this assay that is causative for primary hyperoxalura is AGXT (primary hyperoxaluria type 1). If there remains concern for primary hyperoxaluria types 2 and 3, consideration could be give to additional testing for pathogenic variants in the GRHPR and HOGA1 genes, respectively. 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; reportable variants are confirmed by Sanger sequencing:
NONE

This result has been reviewed and approved by [redacted]

BACKGROUND INFORMATION: Peroxisomal Disorders Panel, Sequencing

CHARACTERISTICS: Peroxisomal disorders are a group of diseases caused by gene defects impairing the formation (peroxisome biogenesis disorders) or function of the peroxisomes, with symptoms that impact a wide range of body systems. Peroxisome biogenesis disorders include Zellweger spectrum disorders (ZSD)

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

and rhizomelic chondrodysplasia punctata (RCDP). Single enzyme defects include Refsum disease, peroxisomal acyl-CoA oxidase deficiency, peroxisomal bifunctional deficiency, defects of bile acid synthesis, and primary hyperoxaluria. Some single enzyme defects present with similar clinical features to ZSD (e.g. ACOX1, HSD17B4) or RCDP (e.g. AGPS, GNPAT), although these often can be distinguished by extensive biochemical testing. Signs and symptoms of peroxisomal disorders may develop as early as the newborn period, with hypotonia, seizures, poor growth, and feeding problems. Leukodystrophy, hepatic dysfunction, adrenal insufficiency, hearing loss, and visual impairment may also be present. Skeletal abnormalities in individuals with peroxisomal disorders include stippling of the growth plates and chondrodysplasia punctata, or progressive loss of bone mineral density. Later onset forms of these conditions have similar symptoms, but with a slower progression and milder severity. Developmental delay and intellectual disability are common.

INCIDENCE: Approximately 1 in 50,000

CAUSE: Pathogenic germline variants in genes associated with the structure and function of peroxisomes.

INHERITANCE: Autosomal recessive with rare autosomal dominant cases

CLINICAL SENSITIVITY: At least 97% for Zellweger spectrum disorders
At least 97% for rhizomelic chondrodysplasia punctata

GENES TESTED: ABCD3, ACBD5*, ACOX1, AGPS, AGXT, AMACR, DNM1L, FAR1, GNPAT, HSD17B4, PEX1, PEX10, PEX11B, PEX12, PEX13, PEX14, PEX16, PEX19, PEX2, PEX26, PEX3, PEX5, PEX6, PEX7, PHYH, SCP2*

* One or more exons are not covered by sequencing for the indicated gene; see limitations section below.

METHODOLOGY: 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.

ANALYTICAL SENSITIVITY/SPECIFICITY: The analytical sensitivity of this test is approximately 99 percent for single nucleotide variants (SNVs) and greater than 93 percent for insertions/duplications/deletions from 1-10 base pairs in size. Variants greater than 10 base pairs may be detected, but the analytical sensitivity may be reduced.

LIMITATIONS: A negative result does not exclude a diagnosis of peroxisomal disorders. This test only detects variants within the coding regions and intron-exon boundaries of the targeted genes. Regulatory region variants and deep intronic variants will not be identified. Deletions/duplications/insertions of any size may not be detected by massively parallel sequencing. Diagnostic errors can occur due to rare sequence variations. In some cases, variants may not be identified due to technical limitations in the presence of pseudogenes, repetitive, or homologous regions. This assay may not detect low-level mosaic or somatic variants associated with disease. Interpretation of this test result may be impacted if this patient has had an allogeneic stem cell transplantation. Non coding transcripts were not analyzed.

The following regions are not sequenced due to technical limitations of the assay:
ACBD5 (NM_001352568) exon(s) 6
ACBD5 (NM_001352569) exon(s) 6
ACBD5 (NM_001352570) exon(s) 13
ACBD5 (NM_001352571) exon(s) 5
ACBD5 (NM_001352573) exon(s) 6
ACBD5 (NM_001352574) exon(s) 6

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ACBD5 (NM_001352575) exon(s) 6
ACBD5 (NM_001352576) exon(s) 6
ACBD5 (NM_001352581) exon(s) 6
ACBD5 (NM_001352585) exon(s) 5
ACBD5 (NM_001352586) exon(s) 5
ACBD5 (NM_001352568) partial exon(s) 1(Chr10:27529638-27529648)
ACBD5 (NM_001352572) partial exon(s) 1(Chr10:27529638-27529648)
SCP2 (NM_001007098) exon(s) 11
SCP2 (NM_001330587) exon(s) 12

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
Peroxisomal Disorders Specimen	22-061-403516	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Peroxisomal Disorders Interp	22-061-403516	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