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

Physician: Doctor, Example

Patient: Patient, Example

DOB	3/11/2018
Gender:	Male
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	00/00/0000 00:00

Exome Sequencing, Proband

ARUP test code 2006336

Exome Sequencing Specimen, Patient: Whole Blood

Exome Sequencing Interpretation, Patient: Negative

TEST PERFORMED
Exome Sequencing, proband only

RESULT
Negative. No variants were identified that are predicted to be causative for the patient's phenotype.

INDICATION FOR TESTING
According to information provided to ARUP Laboratories, the patient is a 34 month old white male with a diagnosis of fetal alcohol syndrome and suspected diagnosis of chondrodysplasia. He has IUGR, stiff joints, hypotonia and muscle weakness, global developmental delay, multicystic dysplastic left kidney, undescended testes, nystagmus. He had a secundum ASD and PDA. His distinctive features include severe midface hypoplasia, hypoplastic nose, large ears, bilateral ptosis, epicanthal folds, prominent brow and plagiocephaly (treated with helmet). He was born vaginally at 37 weeks 3 days gestation, Apgars were 8 and 9, height and weight were less than the 1st percentile and OFC was at the 2nd percentile. He required ventilatory support and treatment for withdrawals from methamphetamine, heroin, and alcohol. He had a strangulated inguinal hernia that required surgical repair and difficulty feeding resulting in chronic aspirations requiring G-tube placement. An echo revealed a hole in the heart that has since resolved. He was discharged from NICU at 3 months of age but readmitted soon after requiring BiPAP. Due to worsening feeding intolerance he required a Nissen fundo procedure. Respiratory insufficiency has improved so now he only requires occasional BiPAP while sleeping. He has had periodic regression usually following a severe illness/ hospitalization. He is currently less than 3rd percentile for height, weight, and OFC (44.2 cm). He began crawling at 24 months, pulling to stand at 27 months, understands simple commands and uses 2-3 words. X-ray of cervical spine showed underdevelopment of multiple cervical vertebra most pronounced from C4-C7. Previous normal testing has included: genomic SNP microarray, chromosome analysis, VLCFA, CMV, bilirubin, reticulocytes, brain MRI, chondrodysplasia punctata 10 gene panel, skeletal dysplasia 109 gene panel (one VUS in ACP5 c.766G>C; p.Val256Leu). He has lived with his adoptive mother since age 3 months. He has a full 6 month old sister with mild feeding difficulties and 4 maternal half-brothers. His biological mother has pancreatitis and breast cancer.

INTERPRETATION

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

A cause for the patient's condition could not be identified.

The ACP5 c.766G>C; p.Val256Leu variant detected by prior gene panel testing was also identified by this exome analysis. Based on the limited available information, the clinical significance of this variant is uncertain. Pathogenic variation in ACP5 is typically associated with spondyloenchondrodysplasia with immune dysregulation (MIM: 607944), a disorder with phenotypic features that do not resemble those of the patient in this case. No other rare variants were identified in ACP5.

No pathogenic variants were identified in 2394 genes that were reviewed related to the following HPO terms: HP:0000028 (Cryptorchidism), HP:0001263 (Global developmental delay), HP:0000023 (Inguinal hernia), HP:0001511 (Intrauterine growth retardation), HP:0011800 (Midface retrusion), HP:0000003 (Multicystic kidney dysplasia), HP:0001324 (Muscle weakness), HP:0001252 (Muscular hypotonia), HP:0000639 (Nystagmus), HP:0011041 (Aplasia/hypoplasia of the cervical spine), HP:0000252 (Microcephaly); HP:0002093 (Respiratory insufficiency), HP:0002652 (Skeletal dysplasia). Please note that adequate sequencing coverage has not been verified for each of these genes.

No secondary pathogenic variants were detected in the list of genes that the American College of Medical Genetics and Genomics (ACMG) recommends reporting in all individuals undergoing exome sequencing; note that single pathogenic variants in recessive ACMG genes are not reported. A list of ACMG genes are included in the background information. These genes are evaluated only to the extent that standard exome sequencing allows.

RECOMMENDATIONS
Medical management and screening should rely on clinical findings. Genetic consultation and surveillance is recommended.

NOTES
Approximately 95.5% of bases in the coding exome were covered by more than 10 sequencing reads.

This result has been reviewed and approved by [redacted]

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BACKGROUND INFORMATION: Exome Sequencing, Proband

CHARACTERISTICS: The purpose of exome sequencing is to determine the patient's diagnosis when a genetic condition is suspected. The exome includes all known human genes and accounts for approximately 1-2 percent of the human genome. However, it is estimated that the exome harbors approximately 85 percent of genetic disease-causing variants.

CLINICAL SENSITIVITY: A diagnosis is determined in up to 35 percent of patients when parental samples are submitted for targeted sequencing and in 20 percent of cases when parental samples are unavailable.

METHODOLOGY: Targeted capture of all (or selected) coding exons and exon-intron junctions of the targeted genes, followed by massively parallel sequencing. Sanger sequencing was performed as necessary to confirm reported variants. Human genome build 19 (Hg 19) was used for data analysis.

ANALYTICAL SENSITIVITY: The analytical sensitivity of this test is approximately 98 percent for single nucleotide variants (SNVs) and greater than 93 percent for Insertions / duplications / deletions from 1-10 base pairs in size. Deletions/duplication greater than 10 base pairs may be detected, but the analytical sensitivity may be reduced.

LIMITATIONS OF ANALYSIS: A negative result does not exclude all genetic diagnoses. The human exome is not able to be completely analyzed as some genes have not been identified while others, due to technical limitations, cannot either be sequenced or interpreted. Some pathogenic variants reside in regions outside the exome. This test only detects variants within the coding regions and intron-exon boundaries of the targeted genes. Mitochondrial DNA is not analyzed. Chromosomal phase of identified variants may not be determined. 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 somatic variants associated with disease.

LIMITATIONS FOR REPORTING AND INTERPRETATION: Only variants in genes suspected to be associated with the patient's symptoms are reported, with the exception of secondary pathogenic findings, if elected. Additionally, de novo and/or rare compound heterozygous variants in genes of unknown clinical relevance may be reported. Incorrect reporting of biological relationships among family members may affect result interpretation. Mode of inheritance, reduced penetrance, and genetic heterogeneity could reduce clinical sensitivity. Interpretation of this test result may be impacted if this patient has had an allogeneic stem cell transplantation.

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.

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VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
Exome Sequencing Specimen, Patient	21-025-401437	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Exome Sequencing Interpretation, Patient	21-025-401437	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00

END OF CHART

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