Client: ARUP Example Report Only
500 Chipeta Way
Salt Lake City, UT 84108
UNITED STATES

Physician: TEST,

Patient: NEGATIVE, EXOME PRO

DOB
Sex: Female
Patient Identifiers: 51719
Visit Number (FIN): 52106
Collection Date: 8/21/2023 07:38

Exome Sequencing

ARUP test code 3016583

EXOME PRO Int

Negative

TEST PERFORMED
Exome Sequencing
Samples tested: Proband and both parents

RESULT
Primary findings: Negative

KEY CLINICAL FINDINGS
Absence seizure, joint hypermobility, tortuous cerebral arteries, and cortical dysplasia.

HPO terms used: HP:0002121 (absence seizure), HP:0001382 (joint hypermobility), HP:0004938 (tortuous cerebral arteries), HP:0002539 (cortical dysplasia).

INTERPRETATION
A unifying cause for the patient's condition could not be identified. Variants that may be related to the reported phenotype are listed below.

SLC4A9 gene, de novo variant of uncertain significance, unknown inheritance pattern
STARD9 gene, de novo variant of uncertain significance, autosomal recessive inheritance

RARE VARIANTS OF UNCERTAIN SIGNIFICANCE
The following are rare de novo variants in genes with unknown significance/inheritance pattern:

Gene: SLC4A9 (NM_031467.2)
Variant: c.1925C>A; p.Ser642Tyr, heterozygous
Chr5(GRCh37):g.139745761
Frequency: not in gnomAD
Computational prediction programs: Deleterious (REVEL: 0.795)

Gene: STARD9 (NM_020759.2)
Variant: c.11275G>A; p.Val3759Met, heterozygous
Chr15(GRCh37):g.42985051
Frequency: not in gnomAD
Computational prediction programs: Neutral (REVEL: 0.055)

Consent was not provided for reporting of secondary pathogenic variants in the list of genes that the American College of Medical Genetics and Genomics (ACMG) recommends reporting in all individuals undergoing exome sequencing (Miller, 2022).

RECOMMENDATIONS
Medical management and screening should rely on clinical

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

findings. Genetic consultation and surveillance of the medical literature for new information regarding the identified variants and genes are recommended.

NOTES
Approximately 95.5% of bases in the coding exome were covered by more than 10 sequencing reads.
Deep intronic variants, variants in the untranslated regions and large deletions/duplications are not analyzed by this method; therefore, additional variants in the reported genes have not been excluded.
Unless otherwise specified, confirmation by Sanger sequencing was not performed for variants with acceptable quality metrics.

REFERENCES
Miller DT, et al. ACMG SF v3.1 list for reporting of secondary findings in clinical exome and genome sequencing: a policy statement of the American College of Medical Genetics and Genomics (ACMG). Genet Med. 2022;24(7):1407-1414. PMID: 35802134.

This result has been reviewed and approved by

BACKGROUND INFORMATION: Exome Sequencing

CHARACTERISTICS: The purpose of exome sequencing is to determine the patient's diagnosis when a Mendelian genetic condition is suspected. The exome includes all known nuclear 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: Varies based on clinical testing indication, previous clinical evaluations, and availability of parental control samples. A diagnosis is determined in 30-35 percent of patients when parental samples are submitted as exome sequencing controls. Diagnostic rates decrease to approximately 20 percent when parental samples are unavailable.

CLINICAL SENITIVITY: Varies based on clinical testing indication, previous clinical evaluations, and availability of parental control samples. A diagnosis is determined in approximately 20-40% of individuals; higher diagnostic rates are reported when parental samples are submitted as exome sequencing controls. Mode of inheritance, reduced penetrance, and genetic heterogeneity can reduce clinical sensitivity.

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. Regulatory region variants, deep intronic variants, and large deletions/duplications will not be identified. 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. 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 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.

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
EXOME PRO Int	23-233-100747	8/21/2023 7:38:00 AM	8/21/2023 7:39:52 AM	8/21/2023 7:42:00 AM

END OF CHART

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