ARUP LABORATORIES | aruplab.com
500 Chipeta Way, Salt Lake City, Utah 84108-1221
phone: 801-583-2787, toll free: 800-522-2787
Jonathan R. Genzen, MD, PhD, Chief Medical Officer

PATIENT REPORT

Patient Age/Sex: Female

Specimen Collected: 01-May-23 14:12

Whole Genome Sequencing **|Received: 01-May-23 14:12** **Report/Verified: 01-May-23 14:14**

Procedure	Result	Units	Reference Interval
WGS NGS Int	Negative [f1 i1]		

Result Footnote

f1: WGS NGS Int
TEST PERFORMED
Whole Genome Sequencing
Samples tested: Proband and both parents

RESULT
Primary findings: Negative
Secondary findings: Negative

KEY CLINICAL FINDINGS
Abnormality of eye movement, abnormal cerebellar vermis morphology, abnormal head movements, cerebellar dysplasia, neurodevelopmental delay.

HPO terms used:
HP:0000496 (abnormality of eye movement), HP:0002334 (abnormal cerebellar vermis morphology), HP:0002457 (abnormal head movements), HP:0007033 (cerebellar dysplasia), HP:0012758 (neurodevelopmental delay).

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

No secondary pathogenic variants were detected in the v3.1 list of genes that the American College of Medical Genetics and Genomics (ACMG) recommends reporting in all individuals undergoing genome sequencing (Miller, 2022). A list of ACMG genes is included in the additional technical information. These genes are evaluated only to the extent that standard genome sequencing allows. Single pathogenic variants in autosomal recessive ACMG genes are not reported.

RECOMMENDATIONS
Medical management and screening should rely on clinical findings. Genetic consultation is recommended. If after one year from report date clinical suspicion remains high for a genetic etiology, a reanalysis may be ordered, for a fee, though ARUP using these original sequencing data (Whole Genome Reanalysis, ARUP test 3005939).

NOTES
99.3% of bases in the targeted genome were covered by more than 20 sequencing reads.

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.

Test Information

i1: WGS NGS Int
BACKGROUND INFORMATION: Whole Genome Sequencing

CHARACTERISTICS: The purpose of whole genome sequencing is to determine the patient's diagnosis when a genetic condition is suspected. The analyzed genome includes exons from all known human nuclear genes and all intronic variants

Test Information

i1: WGS NGS Int

suspected of influencing splicing. Parental samples are recommended for interpretation of results.

CLINICAL SENSITIVITY: Varies based on clinical symptoms, family history, inheritance pattern, and previous clinical evaluations.

METHODOLOGY: Genomic DNA is extracted from whole blood, prepared into libraries, then sequenced by massively parallel sequencing (MPS; also known as next generation sequencing [NGS]). Variant calling is performed using a custom bioinformatics pipeline that includes phenotype-based scores. Human genome build 19 (Hg 19) is used for data analysis.

ANALYTICAL SENSITIVITY: The analytical sensitivity of this test is 98.6 percent for single nucleotide variants (SNVs). Analytical sensitivity is 97.4 percent for insertions/duplications /deletions ranging in size from 1-15 bp, and 92.0 percent for those 16-50 bp in size.

LIMITATIONS OF ANALYSIS: A negative result does not exclude all genetic diagnoses. The human genome is not able to be completely analyzed as some genes have not been identified while others, due to technical limitations, cannot be sequenced or interpreted. Variants in intergenic or deep intronic regions will only be evaluated if an effect on gene expression is predicted via annotation software. Mode of inheritance, reduced penetrance, and genetic heterogeneity can reduce clinical sensitivity. Large deletions/duplications/insertions are not assessed 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. Mitochondrial DNA (mtDNA) is not analyzed. This assay is not designed to detect low-level somatic variants associated with disease. Interpretation of this test result may be impacted if this patient has had an allogeneic stem cell transplantation. Please see Additional Technical Information located at http://ltd.aruplab.com/Tests/Pub/3016493 for more information.

LIMITATIONS FOR REPORTING AND INTERPRETATION: Only variants in genes suspected to be causative of the patient's symptoms are reported, with the exception of secondary pathogenic findings, if elected. Incorrect reporting of biological relationships among family members may affect result interpretation. Mode of inheritance, reduced penetrance, and genetic heterogeneity can 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 U.S. Food and Drug

Test Information

i1: WGS NGS Int

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.

*=Abnormal, #=Corrected, C=Critical, f=Result Footnote, H-High, i-Test Information, L-Low, t-Interpretive Text, @=Performing lab