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PATIENT REPORT

Patient Age/Sex: Female

Specimen Collected: 25-May-23 13:26

Exome Sequencing **|Received: 25-May-23 13:29** **Report/Verified: 25-May-23 13:40**

Procedure	Result	Units	Reference Interval
EXOME PRO Int	See Note [i1]		

Test Information

i1: EXOME PRO Int

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 /

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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.