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

Physician: Doctor, Example

Patient: Patient, Example

DOB	12/31/1752
Sex:	Female
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	00/00/0000 00:00

Rapid Genome Sequencing

ARUP test code 3019947

RWGS PRO Interp **Positive** *

TEST PERFORMED
Rapid Genome Sequencing
Specimens tested: Proband and both parents

INDICATION FOR TESTING
Intrauterine growth restriction, premature birth, microcephaly, cervical rib, cleft palate, atrial septal defect, short neck, micrognathia, thin vermillion, low-set ears, single palmar crease

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RESULT SUMMARY
Primary findings- Related to Phenotype: Hemizygous for a pathogenic variant in RBM10

Secondary Findings: Negative

PRIMARY FINDINGS- RELATED TO PHENOTYPE

RBM10 Variant

Classification: Pathogenic
Gene (Transcript): RBM10 (NM_005676.5)
OMIM(R) disease: TARP syndrome (MIM: 311900; (1))
Mode of Inheritance: X-Linked
Zygosity: Hemizygous
Variant: c.1801C>T; p.Gln601Ter
Inheritance: Maternally Inherited
[GRCh37]ChrX:g.47041576C>T

Hemizygous pathogenic variants in RBM10 are associated with TARP syndrome (Talipes equinovarus, Atrial septal defect, Robin sequence, and Persistence of the left superior vena cava), a neurodevelopmental disorder characterized by variable clinical phenotypes that may include congenital heart defects, Robin sequence, developmental delay/intellectual disability, feeding difficulties, facial dysmorphism, microcephaly, brain anomalies, and distal limb abnormalities (particularly talipes equinovarus) (2-4). The RBM10 c.1801C>T; p.Gln601Ter variant (rs2147198017), to our knowledge, is not reported in the medical literature or gene specific databases. This variant is also absent from the

Genome Aggregation Database (v2.1.1), indicating it is not a common polymorphism. This variant induces an early termination codon and is predicted to result in a truncated protein or mRNA subject to nonsense-mediated decay. Based on available information, this variant is considered to be pathogenic.

This result is consistent with a diagnosis of TARP syndrome in the proband. Because the proband's mother is a heterozygous carrier of the p.Gln601Ter variant, all her offspring have a 50 percent chance of inheriting the variant regardless of sex.

NEGATIVE RESULTS

The following were not identified in the genome data:
-Clinically relevant copy number variants (CNVs) in the nuclear genome related to the patient's reported phenotype.
-Clinically relevant sequence variants in the mitochondrial genome related to the patient's phenotype.
-Homozygous loss of SMN1 exon 7, causative for spinal muscular atrophy.

No secondary findings variants were detected. The American College of Medical Genetics and Genomics (ACMG) recommends analysis of specific, medically actionable secondary findings (SF) genes in all consented individuals undergoing genome sequencing even though these variants may not be related to the indication for testing (5). Although no secondary findings variants involving genes from the ACMG SF v3.3 list (6) were identified in this individual, this result does not exclude the possibility this individual may carry a pathogenic variant involving one of these genes, or another gene that is not included on this list. If there is clinical suspicion or family history of a genetic condition associated with one of the ACMG SF genes, additional targeted testing should be considered as genome sequencing will not identify all pathogenic variants involving these genes. Note that single pathogenic variants in autosomal recessive ACMG SF genes are not generally reported.

RECOMMENDATIONS

- Genetic counseling.
- Testing for the RBM10 variant by targeted molecular analysis for at-risk family members. Please order ARUP test code 3005867, Familial Targeted Sequencing.
- Preimplantation and/or prenatal diagnosis for the identified RBM10 may be offered to the parents of this individual in future pregnancies.

NOTES

98.9% of bases in the targeted genome were covered by more than 20 sequencing reads. Intergenic variants, deep intronic variants not predicted to alter splicing, and chromosomal rearrangements are not analyzed by this method; therefore, additional variants in the reported genes and regions have not been excluded. Refer to the background information for details of limitations.

Health care providers with questions may contact an ARUP genetic counselor at (800) 242-2787 ext. 2141.

References

1: OMIM(R): Copyright (C) 1996 - Present year, Johns Hopkins University All rights reserved.
2: Niceta M, Barresi S, Pantaleoni F et al. TARP syndrome: Long-term survival, anatomic patterns of congenital heart

defects, differential diagnosis and pathogenetic considerations. Eur J Med Genet 2019. PMID: 30189253.
3: Potter AB, O'Brien TD, Kulkarni A et al. Missense variant in RBM10 associated with mild and non-lethal form of TARP syndrome. Clin Genet 2023. PMID: 36932902.
4: Johnston JJ, Sapp JC, Curry C et al. Expansion of the TARP syndrome phenotype associated with de novo mutations and mosaicism. Am J Med Genet A 2014. PMID: 24259342.
5: Miller DT, Lee K, Gordon AS, et al. Recommendations for reporting of secondary findings in clinical exome and genome sequencing, 2021 update: a policy statement of the American College of Medical Genetics and Genomics (ACMG). Genet Med. 2021. PMID: 34012069.
6: Lee K, Abul-Husn NS, Amendola LM et al. ACMG SF v3.3 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 2025. PMID: 40568962.

This result has been reviewed and approved by [redacted]

BACKGROUND INFORMATION: Rapid Genome Sequencing

CHARACTERISTICS: The purpose of rapid whole genome sequencing (RWGS) is to establish a diagnosis when a genetic condition is suspected in acute clinical scenarios. RWGS utilizes next generation sequencing (NGS) to interrogate more than 92 percent of the genome (excluding telomeric and centromeric regions), including the mitochondrial genome. The inclusion of parental samples is strongly recommended for accurate variant interpretation.

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

METHODOLOGY: Genomic DNA is extracted from whole blood or saliva, prepared into libraries, then sequenced by NGS. Variant calling is performed using the Illumina DRAGEN Bio-IT Platform incorporated with a custom bioinformatics pipeline. Human genome build 19 (Hg 19) is used for data analysis. The analytical procedure identifies single nucleotide variants (SNVs), small insertions/deletions, and copy number variants (CNVs) known, or suspected to be, disease-causing.

ANALYTICAL SENSITIVITY: The analytical sensitivity of this assay is 99.2 percent for SNVs, 99.2 percent for insertions/duplications/deletions (indels) ranging in size from 1-15 base pairs (bp), and 96.9 percent for indels 16-50 bp in size. For mitochondrial SNVs with heteroplasmy greater than or equal to 3 percent, analytical sensitivity is 98.4 percent. Analytical sensitivity for CNVs is greater than 99.9 percent for variants 10 kb or larger in size, and 84.6 percent for those 1-10 kb in size.

LIMITATIONS OF ANALYSIS: A negative result does not exclude a genetic diagnosis. Due to technical limitations, some regions of the genome cannot be sequenced or interpreted. SNVs in intergenic or deep intronic regions will only be evaluated if an effect on gene expression is predicted based on annotation software. Diagnostic errors can occur due to rare sequence variations. In some cases, variants may not be identified due to technical limitations related to pseudogenes or repetitive or homologous regions. This assay is not designed to detect somatic variants, mosaic variants, trinucleotide repeats, uniparental disomy, absence of heterozygosity (AOH), or mitochondrial CNVs. This assay is not designed to detect CNVs greater than 50 bp but less than 1 kb in size. See Additional Technical Information located at http://ltd.aruplab.com/Tests/Pub/3019947 for more information on whole genome sequencing.

REPORTING CONSIDERATIONS: Variant interpretation and reporting is limited to variants known or predicted to have an impact on gene expression. Mitochondrial variant reporting is limited to SNVs with heteroplasmy greater than or equal to 10 percent. Heteroplasmy may vary across tissue types; therefore, reported levels reflect only the tested sample. Variable penetrance and genetic heterogeneity may impact clinical sensitivity. Reported variants are limited to those known or suspected to be causative of the patient's phenotype. Patients may opt in for reporting of secondary pathogenic/likely pathogenic findings, including those involving medically actionable genes on the ACMG Secondary Findings Gene List located at http://ltd.aruplab.com/Tests/Pub/3019947. This gene list is updated periodically and is only accurate for this sample at the time of reporting. Absence of parental data, whether through non-submission, technical failure, or misattributed parentage, will impact interpretation of proband results. Likewise, interpretation of test results may be impacted if any of the tested individuals have undergone 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.

EER RWGS PRO

EERUnavailable

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
RWGS PRO Interp	25-323-105561	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
EER RWGS PRO	25-323-105561	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