Patient ID	Patient Name		Birth Date	Gender	Age
C7028846-0001000	HHLP, TESTING		1991-06-05	M	29
Order Number	**Client Order Number**	**Ordering Physician**	**Report Notes**		
M163922927	M163922927	unknown			
Account Information		**Collected**			
C7028846 DLMP Rochester		05 Nov 2020 09:00			

Result Summary

Pathogenic Variant Detected

Result

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Gene	Amino Acid Change	DNA Change	Genomic Position	Zygosity	Classification
GJB2	p.G12Vfs*2 (p.Gly12Valfs*2)	c.35del	Chr13:20763686	Homozygous	**PATHOGENIC**

The following homozygous PATHOGENIC variant was identified:
GJB2, p.G12Vfs*2 (p.Gly12Valfs*2), c.35del, Chr13:20763686

No additional reportable variants were detected within all other tested genes. See the Method section for a complete list of genes evaluated by this assay.

Interpretation

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GJB2 c.35del (p.Gly12Valfs*2)
The homozygous c.35del (p.Gly12Valfs*2) frameshift variant in the GJB2 gene (MIM:#220290) is an established pathogenic variant.

The c.35del (p.Gly12Valfs*2) variant in the GJB2 gene has been associated with autosomal recessive deafness 1A (DFNB1A) (1). This result is supportive of a diagnosis of autosomal recessive deafness 1A for this individual. Clinical correlation is recommended.

This result should be interpreted in the context of clinical findings, family history, and other laboratory testing.

Consultation with a genetics professional is recommended for interpretation of this result and to determine whether familial testing may be of benefit to this family. Genetic testing for family members is available by ordering FMTT / Familial Mutation, Targeted Testing for the specific variant(s) detected. Please contact the laboratory at 1–800–533–1710 or the online test catalog at www.mayocliniclabs.com for information about FMTT.

REFERENCES

1) Smith RJH, Jones MKN. Nonsyndromic Hearing Loss and Deafness, DFNB1. In: Adam MP, Ardinger HH, Pagon RA, et al., eds. GeneReviews. Seattle (WA): University of Washington, Seattle; September 28, 1998.(PMID20301449)

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Additional Information

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Variant nomenclature is based on the following GenBank Accession numbers (build GRCh37 (hg19)): GJB2 NM_004004.5.

Specimen

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WB Whole Blood

Method

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Evaluation of 160 genes associated with hereditary hearing loss:

ABHD12, ACTG1, ADCY1, ADGRV1 (GPR98), AIFM1, ALMS1, ATP6V1B1, BCS1L, BDP1, BSND, BTD, CABP2, CACNA1D, CATSPER2, CCDC50, CD164, CDC14A, CDH23, CEACAM16, CEP78, CHD7, CIB2, CISD2, CLDN14, CLIC5, CLPP, CLRN1, COCH, COL2A1, COL4A3, COL4A4, COL4A5, COL4A6, COL9A1, COL9A2, COL9A3, COL11A1, COL11A2, CRYM, DCDC2, DFNA5 (GSDME), DIABLO, DIAPH1, DIAPH3, DNMT1, DSPP, EDN3, EDNRB, ELMOD3, EPS8, EPS8L2, ESPN, ESRRB, EYA1, EYA4, FGF3, FGFR2, FLNA, FOXC1, FOXI1, GATA3, GIPC3, GJB2, GJB6, GPSM2, GRHL2, GRXCR1, GRXCR2, HARS2, HGF, HOMER2, HOXA2, HSD17B4, ILDR1, JAG1, KARS, KCNE1, KCNJ10, KCNQ1, KCNQ4, KITLG, LARS2, LHFPL5, LOXHD1, LRTOMT, MARVELD2, MCM2, MET, MIR96, MITF, MSRB3, MT-RNR1, MT-TS1, MYH14, MYH9, MYO3A, MYO6, MYO7A, MYO15A, NARS2, NF2, NLRP3, OPA1, OSBPL2, OTOA, OTOF, OTOG, OTOGL, P2RX2, PAX3, PCDH15, PDZD7, PEX1, PEX6, PHYH, PJVK (DFNB59), PNPT1, POLR1C, POLR1D, POU3F4, POU4F3, PRPS1, PTPN11, PTPRQ, RDX, RIPOR2 (FAM65B), S1PR2, SERPINB6, SIX1, SLC17A8, SLC22A4, SLC26A4, SLC26A5, SLC52A2, SLC52A3, SLITRK6, SMPX, SNAI2, SOX10, STRC, SYNE4, TBC1D24, TCOF1, TECTA, TIMM8A, TJP2, TMC1, TMEM132E, TMIE, TMPRSS3, TNC, TPRN, TRIOBP, TWNK (C10orf2), USH1C, USH1G, USH2A, WBP2, WFS1, and WHRN

Next generation sequencing (NGS) and/or Sanger sequencing was performed to test for the presence of variants in coding regions and intron/exon boundaries of the genes analyzed. NGS and/or a PCR-based quantitative method was performed to test for the presence of deletions and duplications in the genes analyzed.

Due to high homology with pseudogenes, or other regions in the genome, variant detection sensitivity may be decreased in the following genes: ACTG1, ADCY1, CATSPER2, DNMT1, DSPP, ESPN, FOXC1, FOXI1, KARS, OTOA, POU3F4, PTPN11, PTPRQ, SLC22A4, SLC52A2, SOX10, TIMM8A, TPRN, and TRIOBP. There are regions in the DNMT1, DSPP, HOMER2, OTOA, PTPRQ, and STRC genes that cannot be effectively analyzed for the presence of large deletions and/or duplications as a result of technical limitations of the assay, including regions of homology, high GC-rich content, and repetitive sequences.

Disclaimer

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Clinical Correlations
If testing was performed because of a clinically significant family history it is often useful to first test an affected family member. Detection of a reportable variant(s) in an affected family member would allow for more informative testing of at risk individuals.

To discuss the availability of further testing options or for assistance in the interpretation of these results, Mayo Clinic Laboratory genetic counselors can be contacted at 1–800–533–1710.

Technical Limitations
Next generation sequencing may not detect all types of genomic variants. In rare cases, false negative or false positive results may occur. The depth of coverage may be variable for some target regions, but assay performance below the minimum acceptable criteria or for failed regions will be noted. Absence of the mitochondrial variants MT-RNR1 m.1494C>T, MT-RNR1 m.1555A>G, or MT-TS1 m.7445A>G on the report does not rule out the presence of these variants below the limits of detection of this assay (<5% heteroplasmy). Given these limitations, negative results do not rule out the diagnosis of a genetic disorder. If a specific clinical disorder is suspected, evaluation by alternative methods can be considered.

There may be regions of genes that cannot be effectively amplified for sequencing or deletion and duplication analysis as a result of technical limitations of the assay, including regions of homology, high GC content, and repetitive sequences. Confirmation of select reportable variants was performed by

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alternate methodologies based on internal laboratory criteria.

Additionally, low level mosaic variants may not be detected.

This test is not designed to differentiate between somatic and germline variants. If there is a possibility that any detected variant is somatic, additional testing may be necessary to clarify the significance of results.

Reclassification of Variants Policy
See www.mayocliniclabs.com
(TEST ID HHLP) for information regarding the laboratory's policy for reclassification of variants.

Variant Evaluation

Variant curation is performed using published ACMG-AMP recommendations as a guideline. Other gene-specific guidelines may also be considered. Variants classified as benign or likely benign are not reported.

Results from in silico evaluation tools may change over time and should be interpreted with caution and professional clinical judgment.

Released By MCR

Nicole J. Boczek, Ph.D.

Received: 05 Nov 2020 12:42 **Reported:** 06 Nov 2020 09:06

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