

Whole Exome Sequencing: Proband
PROBAND REPORT



Patient Name	Sex Assigned at Birth	DOB	MRN #	Accession #	Lab #

CLINICAL INDICATION

Based on the submitted clinical information, the individual has fatigue, diabetes mellitus, recurrent urinary tract infections, hypertension, hyperlipidemia, atelectasis, pulmonary embolism, and third degree atrioventricular block.

Ordering Provider

Recipient
Facility
Location
Phone #

RESULTS

Test Information

Test Code
Sample TypeBUCCAL SWAB
Family #
Date Collected05.19.2026
Date Received05.20.2026
Date Reported06.10.2026

PRIMARY FINDINGS
Positive - See Results Summary section below.

ACMG SECONDARY FINDINGS
Negative - None Detected.

INCIDENTAL FINDINGS
Negative - None Detected.

RESULTS SUMMARY

A variant in the HSPB8 gene was detected, which is associated with myofibrillar myopathy type 13 with rimmed vacuoles.

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VARIANT FINDINGS

Disease	Inheritance Pattern	Gene / Variant	Genotype	Variant Type	Inherited From	Variant Classification
PRIMARY FINDINGS						
Myopathy, myofibrillar, 13, with rimmed vacuoles	Autosomal Dominant	HSPB8: c.515dup, p.P173Sfs*43	Heterozygous	Sequence Variant	Unknown	Pathogenic

RECOMMENDATIONS

- It is recommended that correlation of these findings with the clinical phenotype be performed.
- Genetic counseling is recommended.
- For sequencing variants, testing is available at charge for this individual's relatives under test code 1580 (Test Catalog - Baylor Genetics. visit: <https://catalog.baylorgenetics.com/details/1580>)
- For sequencing variants meeting certain criteria, test codes 1593 (Familial Variant Testing Policy - Baylor Genetics. visit: <https://www.baylorgenetics.com/familial-variant-testing-policy/>), and 1594 (Variant Resolution Testing Policy - Baylor Genetics. visit: <https://www.baylorgenetics.com/variant-resolution-testing-policy/>) are also available.
- Contact laboratory for requests regarding reanalysis and raw data.
- If you have a question about this report, please call 800-411-4363 or email info@baylorgenetics.com.

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PRIMARY FINDINGS

HSPB8: (NM_014365.3) c.515dup, p.P173Sfs*43

Disease	Inheritance Pattern	Gene / Variant	Genotype	Variant Type	Inherited From	Variant Classification
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DISEASE DESCRIPTION

Pathogenic variants in the HSPB8 gene are associated with autosomal dominant myofibrillar myopathy type 13 with rimmed vacuoles (OMIM: 621078), which is characterized by progressive muscle weakness, muscle atrophy, and muscle fiber degeneration, often with distal predominance. Additional features may include muscle cramps or fasciculations, involvement of proximal or axial muscles, and skeletal abnormalities such as pes cavus, scoliosis, or lumbar lordosis. Age of onset may vary and can range from childhood to adulthood. The condition demonstrates variable expressivity (PMID: 40243504). Current evidence supports a gain-of-function mechanism of disease, although haploinsufficiency cannot be entirely ruled out (PMID: 28501893, 28780615, 36854646). Other pathogenic variants in the HSPB8 gene are associated with autosomal dominant distal hereditary motor neuronopathy type 2 (OMIM: 158590) and autosomal dominant axonal Charcot-Marie-Tooth disease type 2L (OMIM: 608673).

VARIANT DETAILS - HSPB8: (NM_014365.3) c.515dup, p.P173Sfs*43

- The c.515dup (p.P173Sfs*43) variant in the HSPB8 gene has been described as likely pathogenic in ClinVar (ID: 986227). This variant has been previously reported in a heterozygous state in individuals with myofibrillar myopathy with rimmed vacuoles (PMID: 26718575, 31403083).
- This variant has not been observed in the gnomAD v2 dataset.
- Functional studies demonstrate this variant causes aggregate formation and protein mislocalization (PMID: 36854646, 31403083).
- This frameshift variant in exon 3 of 3 is predicted to escape nonsense-mediated decay (NMD) and extend the protein, potentially disrupting normal protein function. Other C-terminal frameshift variants predicted to extend the protein have been reported in individuals with myofibrillar myopathy with rimmed vacuoles (PMID: 28501893, 33744911, 40467930).

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QUALITY METRICS

98.72% Percentage depth of coverage at 20x

186.07x Mean depth of coverage

METHODOLOGY

Genomic DNA was fragmented and indexed to prepare individual libraries. The libraries were enriched by hybridizing to in-solution exome probes, purified, and pooled for sequence analysis on an Illumina platform for paired-end read sequencing. Internal quality control measures are performed to ensure sample integrity.

Data analysis and interpretation are performed by the Baylor Genetics analytics pipeline. Data are aligned to the human reference genome build GRCh37 (HG19) using the Illumina Dragen BioIT Platform. Variant calling is performed using the Illumina Dragen haplotype-based variant calling system and Illumina Dragen genome wide depth based CNV (Copy Number Variants) caller with custom modifications from Baylor Genetics.

The automated genetic interpretation platform from Emedgene is implemented for variant annotation and interpretation with proprietary algorithms and open-source data sets such as gnomAD, EVS (Exome Variant Server), ClinVar and professional resources such as HGMD (Human Gene Mutation Database) Pro. The variants were interpreted according to ACMG (American College of Medical Genetics) guidelines (reference 1) and patient phenotypes.

Variants are confirmed by Sanger sequencing, specific PCR, Multiplex Ligation-dependent Probe Amplification (MLPA), or another methodology, if the sequencing or copy number variants detected by NGS do not meet internal quality standards or are within highly homologous regions.

Synonymous variants, noncoding variants not affecting splicing sites (coding region +/- 20bp), and common benign variants are excluded from interpretation unless previously reported in the literature as possibly pathogenic variants. This test may not provide detection of certain variants or portions of certain genes due to insufficient sequencing depth, local sequence characteristics, high/low genomic complexity, or the presence of closely related pseudogenes. Small deletions or insertions larger than 25bp, heterozygous copy number variants smaller than 100kb or three exons, low-level mosaic variants, structural variants such as inversions and/or balanced translocations may not be detected with this technology. Mitochondrial DNA (mtDNA), short tandem repeats (STR), uniparental disomy (UPD), regions of homozygosity (ROH), and imprinting defects are not analyzed.

The proband report contains results related to the patient's clinical phenotype. Variants relevant to the phenotype are reported as positive (pathogenic/likely pathogenic) or variants of uncertain significance (VUS). Benign and likely benign variants are not reported. This interpretation is based on the clinical information provided by the referring institution and our current understanding of the gene and variants at the time of reporting. Additional methodologies may be used to aid in variant interpretation. Results in the report should be carefully correlated to the individual's clinical findings by the referring physician.

If elected, secondary findings including pathogenic and likely pathogenic variants in genes included in the ACMG secondary findings recommendations, or other findings determined to be severe and medically significant (incidental findings), will be reported. The ACMG recommendations (ACMG SF v3.3 (reference 2)) include the following genes: ABCD1, ACTA2, ACTC1, ACVRL1, APC, APOB, ATP7B, BAG3, BMPR1A, BRCA1, BRCA2, BTBD, CACNA1S, CALM1, CALM2, CALM3, CASQ2, COL3A1, CYP27A1, DES, DSC2, DSG2, DSP, ENG, FBN1, FLNC, GAA, GLA, HFE, HNF1A, KCNH2, KCNQ1, LDLR, LMNA, MAX, MEN1, MLH1, MSH2, MSH6, MUTYH, MYBPC3, MYH11, MYH7, MYL2, MYL3, NF2, OTC, PALB2, PCSK9, PKP2, PMS2, PLN, PRKAG2, PTEN, RB1, RBM20, RET, RPE65, RYR1, RYR2, SCN5A, SDHAF2, SDHB, SDHC, SDHD, SMAD3, SMAD4, STK11, TGFBR1, TGFBR2, TMEM127, TMEM43, TNNC1, TNNI3, TNNT2, TP53, TPM1, TRDN, TSC1, TSC2, TTN, TTR, VHL, and WT1. Variants unrelated to the patient's phenotype but potentially clinically significant in genes with no known disease association will be reported if elected.

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[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]

LIMITATIONS

The interpretation of nucleotide changes is based on our current understanding of the specific genes in which those changes occur. This interpretation may change over time as more information about these genes becomes available. Possible diagnostic errors include sample mix-ups, genetic variants that interfere with analysis, incorrect assignment of biological parentage, or other sources. Please contact a genetic counselor at Baylor Genetics if there is reason to suspect one of these sources of error.

REFERENCES

1. Richards S, Aziz N, Bale S, Bick D, Das S, Gastier-Foster J, Grody WW, Hegde M, Lyon E, Spector E, Voelkerding K, Rehm HL; ACMG Laboratory Quality Assurance Committee. Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. Genet Med. 2015 May;17(5):405-24. doi: 10.1038/gim.2015.30. Epub 2015 Mar 5. PMID: 25741868; PMCID: PMC4544753.

2. Lee K, Abul-Husn NS, Amendola LM, Brothers KB, Chung WK, Gollob MH, Gordon AS, Harrison SM, Hershberger RE, Li M, Ondrasik D, Richards CS, Stergachis A, Stewart DR, Martin CL, Miller DT; ACMG Secondary Findings Working Group. (2025). 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). Genetics in Medicine, 27(8), 101454. <https://doi.org/10.1016/j.gim.2025.101454>. PMID: 40568962.

DISCLAIMER

This test was developed, and its performance was determined by the Baylor Miraca Genetics Laboratory DBA Baylor Genetics. It has not been cleared or approved by the U.S. Food and Drug Administration (FDA). Since FDA is not required for clinical use of this test, this laboratory has established and validated the test's accuracy and precision, pursuant to the requirement of CLIA'88. This laboratory is licensed and/or accredited under CLIA and CAP (CAP#2109314 / CLIA# 45D0660090; Lab Director: Christine M. Eng, MD).

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