SAMPLE-Positive Results-Cardiomyopathy and Familial Hypercholesterolemia Panel

Patient	Specimen	Ordering Physician
Patient Name: VINCENT JONES	**Specimen Type:** BS	**Physician:** [redacted]
Date of Birth: [redacted]	**Collection Date:** [redacted]	**Institution:**
Accession ID: [redacted]	**Received Date:** 06/29/2021	**Report Date:** 07/11/2021
Sex: Male		

Indication for Testing

Z82.49

Test Result

Positive Result Pathogenic/Likely pathogenic variant(s) detected.

Primary Findings

GENE	VARIANT	POSITION	ZYGOSITY	CLASSIFICATION
MYBPC3	c.2221del p.Ala741GlnfsTer13	g.47360157GC>G	Heterozygous	Pathogenic

Primary Findings Summary

***MYBPC3* p.Ala741GlnfsTer13**

This patient is heterozygous for variant p.Ala741GlnfsTer13 in the *MYBPC3* gene. This variant is expected to create a premature translational stop codon which in turn would result in absent or decreased protein product. The variant has one submission in Clinvar as pathogenic (SCV000208294). This variant is not present in population databases. Using the above mentioned evidence, it is classified as pathogenic. PP5+PM2+PVS1.

MYBPC3 encodes the cardiac isoform of myosin-binding protein C. Myosin-binding protein C is a myosin-associated protein found in the cross-bridge-bearing zone (C region) of A bands in striated muscle. MYBPC3, the cardiac isoform, is expressed exclussively in heart muscle. Regulatory phosphorylation of the cardiac isoform in vivo by cAMP-dependent protein kinase (PKA) upon adrenergic stimulation may be linked to modulation of cardiac contraction. Mutations in MYBPC3 are one cause of familial hypertrophic cardiomyopathy. [provided by RefSeq, Jul 2008]

Recommendations

- Confirmation by orthogonal technology is recommended and if confirmed, consultation with a genetic counselor or qualified healthcare provider is required to establish definitive risk. This result should be considered preliminary until such confirmation has been performed. Clinical management for this individual should be based on personal and family history, along with other relevant information. If considered relevant to this individual's clinical presentation and/or family history, targeted testing of appropriate family members of this individual for the pathogenic change or variant of unknown significance may help to interpret these results. For more information, please contact the National Society of Genetic Counselors and locate a practitioner near you

Patient

Patient Name: [redacted] **Date of Birth:** [redacted] **Accession ID:** [redacted]

Recommendations (CONT.)

at https://www.nsgc.org/page/find-a-genetic-counselor or by phone at 312.321.6834.

Test results reviewed and approved by:

Owatha Tatum, Ph.D., HCLD/CC(ABB)

Jul 11, 2021

Patient

Patient Name: [redacted] **Date of Birth:** [redacted] **Accession ID:** [redacted]

Test Methodology

Cardiomyopathy Risk Factor Screening (CGx) performed at Advanced Biomedical National Laboratory Services utilizes Next-Generation Sequencing technology using AmpliSeq chemistry on Thermo Fisher Ion S5 GeneStudio Instrumentation. Genomic DNA is extracted from Buccal swabs, then amplified for regions of interest using primers specific for each region. Positive and negative controls are included with each machine run to ensure the accuracy of amplicon preparation and sequencing. Targeted sequencing is performed on coding regions and intronic/exonic boundaries of interest. Exclusions from analysis are listed below. Sequences obtained are then aligned against a human reference genome and variants such as SNVs (Small Nucleotide Variants) and Indels (Insertions and Deletions) are noted.

Variant calling and interpretation are performed by Fabric Genomics. Variants qualified by Advanced Biomedical are analyzed by Fabric variant scientists according to the standards and guidelines for sequence variant interpretation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. (ACMG/AMP; PMID:25741868). Only variants achieving a classification of "Pathogenic" or "Likely Pathogenic" are reported. All reports are reviewed prior to release by either Advanced Biomedical's Medical Director, Technical Supervisor or qualified contracted Scientific Advisor.

Genes Evaluated

ABCC9, ACTA2, ACTC1, ACTN2, ANKRD1, APOB, BAG3, CACNA1C, CACNA2D1, CALM1, CASQ2, CAV3, CRYAB, CSRP3, DES, DMD, DOLK, DSC2, DSG2, DSP, DTNA, ELN, EYA4, FBN1, GATAD1, GPD1L, HCN4, KCND3, KCNE2, KCNH2, KCNJ5, KCNJ8, KCNQ1, LAMP2, LDLR, LDLRAP1, LMNA, MURC, MYBPC3, MYH11, MYH6, MYH7, MYL2, MYL3, MYOZ2, NKX2-5, PCSK9, PKP2, PLN, PRKAG2, RYR2, SCN1B, SCN2B, SCN3B, SCN4B, SCN5A, SCO2, SGCD, SLC25A4, SLC2A10, TAZ, TBX20, TBX5, TCAP, TGFB3, TNNC1, TNNI3, TNNT2, TTN, TTR

Test Limitations

Some variations in these genomic regions may not be reported such as: large genomic rearrangements greater than 50 bp in length, rare (low frequency) mutations, or structural (non-coding) variations. 8 genomic regions were observed to have mean coverage depths that did not meet clinical sufficiency thresholds. These regions are excluded from tertiary analysis and reporting, and include:

chr12--22017258--22017479
chr1--236900429--236900651
chr10--92675790--92676015
chr12--269194--2692164
chr7--81591094--81591278
chr6--7583672--7583898
chr15--73615709--73615942
chr15--73660220--73660411
chr7--150671587--150671817
chr7--150645460--150645692
chr7--150674821--150675058
chr11--2466280--2466436
chr16--15931892--15932072
chr14--23855465--23855692
chr14--23859231--23859468
chr14--23855187--23855378

Patient

Patient Name: [redacted] Date of Birth: [redacted] Accession ID: [redacted]

Test Limitations (CONT.)

chr14--23884786–23885018
chr14--23889228–23889465
chr1–55505476–55505713
chr1–55521757–55521993
chr1–237205673–237205910
chr19--35521685–35521887
chr7–3529292–35293156
chr2–179510688–179510907
chr2–179527827–179528051
chr2–179585274–179585492
chr2–179604620–179604842
chr2–179623724–179623918

Rare diagnostics errors may occur if these mutations occur within the priming sequencing regions. Presence of a pathogenic/likely pathogenic variant does not guarantee that an individual will develop cancer, nor is the absence of such variants a guarantee that an individual will not develop cancer. The results of this screen are meant strictly to guide a physician in the management of their patient's health.

Regulatory Disclosures

Genetic-based hereditary Cardiomyopathy Risk Factor screening is intended as a tool to guide physicians in the management of their patients and should NOT be treated as a diagnostic tool. NGS-based hereditary Cardiomyopathy screening is considered a high-complexity laboratory-developed test (LDT) by CMS under the Clinical Laboratory Improvement Amendment (CLIA) and is not FDA-cleared. The test and performance metrics were validated in house by Advanced Biomedical technical personnel (or designated scientific advisors) and approved by their Laboratory Director. The results are intended for use only by the ordering physician and/or designated healthcare provider. The ordering provider is responsible for 1) ascertaining the medical necessity of the ordered test, 2) resulting diagnoses, 3) management of the disease and/or decisions based on the data provided. Results rely on collection personnel following specified collection and shipment protocols.

Testing was performed by a CLIA facility at 1551 SW 37th Ave, Ocala, FL 34474.

CLIA# 10D2145635, Laboratory Director: Mills Brinson III Technical Supervisor: Ioan Cucoranu, MD, FCAP