

## Cardiomyopathy-Pulmonary Genetic Risk Panel

| Patient        |             | Specimen            |             | Ordering Physician |                 |
|----------------|-------------|---------------------|-------------|--------------------|-----------------|
| First Name:    | Test        | Specimen Type:      | Buccal Swab | Physician:         | Dr. Test        |
| Last name:     | Patient     | Collection Date:    | 06-13-2022  | Institution:       | Test Physicians |
| Date of Birth: | 11-21-9999  | Received Date:      | 06-15-2022  | Reported Date:     | 07-02-2022      |
| Gender:        | Male        | Panel Coverage :    | >=50%       | Ref Accession:     | N/A             |
| Accession ID:  | E2306150497 | Average Read Depth: | >50%        |                    |                 |

### SUMMARY OF RESULTS

**NEGATIVE**

Summary of Result : NEGATIVE

### Recommendations

A negative result indicates that the individual does not have pathogenic or likely pathogenic variants known to be associated with Cardiomyopathy-Pulmonary disease risk from the list of genes evaluated through next generation sequencing (NGS). For more information, please contact the National Society of Genetic Counselors and locate a practitioner near you at <https://www.nsgc.org/page/find-a-genetic-counselor> or by phone at 312.321.6834.

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## Test Methodology

Cardiomyopathy-Pulmonary Disease Risk Factor Screening 242 gene panel screening performed at Ipseity Diagnostics LLC utilizes Next Generation Sequencing (NGS) technology using targeted gene enrichment chemistry on the Illumina® MiniSeq platform. Genomic DNA extracted from Buccal swabs (Dry and Wet) are tagged and enriched for regions of interest using probes specific for each region specified in the BED (Browser Extensible Data) file. Positive ([www.coriell.org](http://www.coriell.org)) and Negative controls are included with each machine run to ensure the accuracy of amplicon preparation alongside targeted sequencing on coding regions and intronic/exonic boundaries of interest and precise finding of the variant on the positive control and negative control respectively. 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. For a detailed list of regions covered and comprehensive statistics by Ipseity Diagnostics LLC Cardiomyopathy-Pulmonary screen, please contact us on Email:[info@ipseity.com](mailto:info@ipseity.com)

Computational analysis and variant calling is performed by ipseity ([www.ipseity.com](http://www.ipseity.com)). Briefly, reads from the sequence output were aligned to the human reference genome (GRCh37) using the Burrows-Wheeler Aligner (BWA). Variants to the reference were called using the Genomic Analysis Tool Kit (GATK). The variants were annotated and filtered using the Ipseity Diagnostics LLC analysis work flow implementing the ACMG guidelines for interpretation of sequence variants. This includes comparison against the gnomAD population catalog of variants in 123,136 exomes, the 1000 Genomes Project Consortium's publication of 2,500 genomes, the NCBI-ClinVar database of clinical assertions on variant's pathogenicity and multiple lines of computational evidence on conservation and functional impact. The following databases and insilico algorithms are used to annotate and evaluate the impact of the variant in the context of human disease: 1000 genomes, gnomAD, ClinVar, OMIM, dbSNP, NCIB Ref Seq Genes, ExAC Gene Constraints, VS-SIFT, VS PolyPhen2, PhyloP, GERP+, GeneSplicer, Max EntScan, NNSplice, PWM Splice Predictor. Analysis was reported using the HGVS nomenclature ([www.hgvs.org/mutnomen](http://www.hgvs.org/mutnomen)) as implemented by custom transcript annotation algorithm. Only variants with an end ACMG classification of "Pathogenic" or "Likely Pathogenic" are reported and VUS/Benign/Likely Benign variants are not reported. Classification of pathogenicity is consistently updated by the National Institutes of Health and the information found within this report is consistent with the current knowledge base as the knowledge base changes, so may clinical interpretation of variants. All reports are reviewed prior to release by either Ipseity Diagnostics LLC's Technical Supervisor or the General Supervisor.

## Genes Evaluated

ABCC9, ACTA2, ACTC1, ACTN2, ACVRL1, ADAMTS2, AKAP9, ALDH18A1, ALMS1, ALPK3, ANK2, ANKRD1, APOB, ATP6V0A2, ATP6V1E1, ATP7A,B3GALT6, B3GAT3, B4GALT7, BAG3, BGN, BMPR2, BRAF, CACNA1C, CACNA2D1, CACNB2, CALM1, CALM2, CALM3, CASQ2, CAV1, CAV3, CBS, CHRM2, CHST14, COL11A1, COL11A2, COL12A1, COL1A1, COL1A2, COL2A1, COL3A1, COL5A1, COL5A2, COL9A1, COL9A2, COL9A3, CRYAB, CSRP3, CTNNA3, DES, DMD, DOLK, DSC2, DSE, DSG2, DSP, DTNA, EFEMP2, EIF2AK4, ELN, EMD, ENG, EYA4, FBLN5, FBN1, FBN2, FHL1, FKBP14, FKRP, FKTN, FLNA, F9, FLNC, GAA, GATA4, GATA5, GATA6, GATAD1, GDF2, GJA5, KCNJ8, KCNK3, KCNQ1, KRAS, LAMA4, LAMP2, LDB3, LDLR, LDLRAP1, LMNA, LOX, LRRC10, LTBP4, MAP2K1, MAP2K2, MAT2A, MED12, MFAP5, MIB1, MURC, MYBPC3, MYH11, MYH6, MYH7, MYL2, MYL3, MYL4, MYLK, MYLK2, MYOZ2, MYPN, NEBL, NEXN, NKX2-5, NOTCH1, NRAS, PCSK9, PDLIM3, PKP2, PLN, PLOD1, PPA2, PRDM16, PRDM5, PRKAG2, PRKG1, PTPN11, PYCR1, RAF1, RANGRF, RASA1, RBM20, RIN2, RIT1, RYR2, SCN10A, SCN1B, SCN2B, SCN3B, SCN4B, SCN5A, SGCD, SHOC2, SKI, SLC2A10, SLC39A13, SMAD2, SMAD3, SMAD4, SMAD9, SNTA1, SOS1, TAZ, TBX20, TCAP, TECRL, TGFB2, TGFB3, TGFB3, TGFB3, TGFB3, TMEM11, TMPO, TNNC1, TNNI3, TNNT2, TNXB, TOR1AIP1, TPM1, TRDN, TRPM4, TTN, TTR, TXNRD2, VCL, ZNF469, CCDC39, CCDC40, CFTR, CHAT, CHRNA1, CHRN1, CHRND, CHRNE, COLQ, CSF2RA, CSF2RB, DKC1, DNAF1, DNAF2, DNAH1, DNAH11, DNAH5, DNAI1, DNAI2, DNAL1, EDN3, EFEMP2, ELMOD2, ELN, FBLN5, FLCN, FOXF1, GAS8, GLRA1, HPS1, HPS4, ITGA3, LTBP4, MECP2, NAF1, NF1, NKX2-1, NME8, PARN, PHOX2B, PIH1D3, RAPSN, RET, RSPH3, RSPH4A, RSPH9, RTEL1, SCNA4, SCNN1A, SCNN1B, SERPINA1, SFTPA1, SFTPA2, SFTPB, SFTPC, SLC34A2, SLC6A5, SLC7A7, SMPD1, STAT3, TERC, TERT, TINF2, TSC1, TSC2, ZEB2.

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## 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 and pseudogenes. These regions are excluded from tertiary analysis and reporting, and include:

chr 1: 237919587-237919687\_RYR2:Exon(254724593)  
chr 1 : 47372052-47372166 MYBPC3:Exon(254724862)  
chr 7 : 7123440-7123516 ACADVL:Exon(254723728)  
chr 17 : 78075354-78075424\_GAA:5'UTRExon(254724327}  
chr 8 : 29078026-29078259\_DSG2:5'UTRExon(254724285)  
chr 9 : 47249302-47249347\_FKRP:5'UTRExon(254725371)  
chr 3 : 38691021 38691164\_SCN5A:5'UTRExon(254724130)  
chr X : 135229558-135229787\_FHL1:5'UTRExon(254724192)  
chr16:2097989:2098066:TSC2:5'UTRExon(254723602)  
chr9:135779797:135779841:TSC1:Exon(254722795)

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 Cardiomyopathy-Pulmonary disease, nor is the absence of such variants a guarantee that an individual will not develop a 'Cardiomyopathy-Pulmonary Disease'. The results of this screen are meant strictly to guide a physician in the management of their patient's health. Any Likely pathogenic or Pathogenic variants detected in the report should be clinically correlated (As per Physicians Advice) and confirmed via the orthogonal testing platforms (Sanger Sequencing or PCR based tests).

## Regulatory Disclosures

Genetics based hereditary Cardiomyopathy-Pulmonary 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 for NGS-based hereditary Cardiomyopathy-Pulmonary 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 Ipseity Diagnostics LLC 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.

## REFERENCES

Richards, Sue, et al. 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. *Genetics in medicine* 17.5 (2015): 405. Exome Aggregation Consortium et al. Analysis of Protein-Coding Genetic Variation in 60,706 Humans. *Nature* 536.7616 (2016): 285–291. PMC. Web. 13 May 2018. The 1000 Genomes Project Consortium. A Global Reference for Human Genetic Variation. *Nature* 526.7571 (2015): 68–74. PMC. Web. 13 May 2018.