

Ordered By Medical: Unknown, Unknown, MD Professional: Client: Ambry Additional Authorized Recipient:	Contact ID:7640651 Org ID:1	Patient Legal Name: Unknown, Unknown Accession #: 01-272292 AP2 Order #: 3625027 Birthdate: 01/01/9999 MRN #: N/A Indication: Internal Testing	Specimen #: Specimen: Blood EDTA (Purple top) Sex assigned at birth: U Collected: 04/06/2026 Received: 04/06/2026 Test Started: 04/06/2026
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CardioNext[®]: Analyses of 92 Genes Associated with Inherited Cardiomyopathies and Arrhythmias

RESULTS

Pathogenic Mutation(s): None Detected
Variant(s) of Unknown Significance: None Detected
Gross Deletion(s)/Duplication(s): None Detected

SUMMARY

NEGATIVE: No Clinically Significant Variants Detected

INTERPRETATION

- No pathogenic mutations, variants of unknown significance, or gross deletions or duplications were detected.
- **Risk Estimate:** low likelihood of variants in the genes analyzed contributing to this individual's clinical history.
- Genetic counseling is a recommended option for all individuals undergoing genetic testing.

Genes Analyzed (92 total): *ABCC9, ACTC1, ACTN2, AKAP9, ALPK3, ANK2, ANKRD1, BAG3, CACNA1C, CACNA2D1, CACNB2, CALM1, CASQ2, CAV3, CRYAB, CSRP3, DES, DMD, DSC2, DSG2, DSP, EMD, EYA4, FKRP, FKTN, FLNC, GATAD1, GLA, GPD1L, HCN4, JPH2, JUP, KCND3, KCNE1, KCNE2, KCNE3, KCNH2, KCNJ2, KCNJ5, KCNJ8, KCNQ1, LAMA4, LAMP2, LDB3, LMNA, MYBPC3, MYH6, MYH7, MYL2, MYL3, MYOZ2, MYPN, NEXN, NKX2-5, PKP2, PLN, PRKAG2, PTPN11, RAF1, RBM20, RYR2, SCN1B, SCN2B, SCN3B, SCN4B, SCN5A, SNTA1, TAZ, TBX20, TBX5, TCAP, TGFB3, TMEM43, TNNC1, TNNI3, TNNT2, TPM1, TRDN, TRPM4, TTN, TTR, TXNRD2* and *VCL* (sequencing and deletion/duplication); *ALMS1, CALM2, CALM3, DOLK, FHL1, RIT1, SCN10A, SOS1* and *TECRL* (sequencing only).

Order Summary: The following products were included in the test order for this individual. Please note: tests on hold and those that have been cancelled (including reflex testing steps cancelled due to a positive result in a preceding test) are excluded. For additional information, please contact Ambry Genetics.

- CardioNext[®] (Product Code 8911)

ELECTRONICALLY SIGNED BY

C. Christopher Lau, Ph.D., FACMG, CGMBS, on 04/09/2026 at 17:12:47 pm

ASSAY INFORMATION

General methodology: Genomic deoxyribonucleic acid (gDNA) is isolated from the patient's specimen using standardized methodology and quantified. Sequence enrichment of the targeted coding exons and adjacent intronic nucleotides is carried out by a bait-capture methodology using long biotinylated oligonucleotide probes followed by polymerase chain reaction (PCR) and Next-Generation sequencing (NGS). Variants in regions complicated by pseudogene interference, variant calls not satisfying depth of coverage and variant allele frequency quality thresholds, and potentially homozygous variants are verified by Sanger sequencing. Gross deletion/duplication analysis is performed using a custom pipeline based on read-depth from NGS data followed by a confirmatory orthogonal method, as needed. Mobile element insertions, if detected, are confirmed by a confirmatory orthogonal method, as needed.

NCBI reference sequences: *ABCC9*-NM_005691.2, *ACTC1*-NM_005159.4, *ACTN2*-NM_001103.2, *AKAP9*-NM_005751.4, *ALMS1*-NM_015120.4, *ALPK3*-NM_020778.4, *ANK2*-NM_001148.4, *ANKRD1*-NM_014391.2, *BAG3*-NM_004281.3, *CACNA1C*-NM_000719.6, *CACNA2D1*-NM_000722.2, *CACNB2*-NM_201590.2, *CALM1*-NM_006888.4, *CALM2*-NM_001743.4, *CALM3*-NM_005184.2, *CASQ2*-NM_001232.3, *CAV3*-NM_033337.2, *CRYAB*-NM_001885.1, *CSRP3*-NM_003476.3, *DES*-NM_001927.3, *DMD*-NM_004006.2, *DOLK*-NM_014908, *DSC2*-NM_024422.3, *DSG2*-NM_001943.3, *DSP*-NM_004415.2, *EMD*-NM_000117.2, *EYA4*-NM_004100.4, *FHL1*-NM_001449, *FKTN*-NM_001079802.1, *FKRP*-NM_024301.4, *FLNC*-NM_001458.4, *GATAD1*-NM_021167.3, *GLA*-NM_000169.2, *GPD1L*-NM_015141.3, *HGN4*-NM_005477.2, *JPH2*-NM_020433.4, *JUP*-NM_002230.2, *KCND3*-NM_004980.4, *KCNE1*-NM_000219.3, *KCNE2*-NM_172201.1, *KCNE3*-NM_005472.4, *KCNH2*-NM_000238.3, *KCNJ2*-NM_000891.2, *KCNJ5*-NM_000890.3, *KCNJ8*-NM_004982.2, *KCNQ1*-NM_000218.2, *LAMA4*-NM_002290.3, *LAMP2*-NM_002294.2, *LDB3*-NM_007078.2, *LMNA*-NM_170707.2, *MYBPC3*-NM_000256.3, *MYH6*-NM_002471.3, *MYH7*-NM_000257.4, *MYL2*-NM_000432.3, *MYL3*-NM_000258.2, *MYOZ2*-NM_016599.4, *MYPN*-NM_032578.2, *NEXN*-NM_144573.3, *NKX2-5*-NM_004387.3, *PKP2*-NM_004572.3, *PLN*-NM_002667.3, *PRKAG2*-NM_016203.3, *PTPN11*-NM_002834.3, *RAF1*-NM_002880.3, *RBM20*-NM_001134363.1, *RIT1*-NM_006912.4, *RYR2*-NM_001035.2, *SCN10A*-NM_006514.3, *SCN1B*-NM_001037.4, *SCN2B*-NM_004588.4, *SCN3B*-NM_018400.3, *SCN4B*-NM_174934.3, *SCN5A*-NM_198056.2, *SNTA1*-NM_003098.2, *SOS1*-NM_005633.3, *TAZ*-NM_000116.3, *TBX5*-NM_000192.3, *TBX20*-NM_001077653.2, *TCAP*-NM_003673.3, *TECRL*-NM_001010874.4, *TGFB3*-NM_003239.2, *TMEM43*-NM_024334.2, *TNNC1*-NM_003280.2, *TNNI3*-NM_000363.4, *TNNT2*-NM_001001430.1, *TPM1*-NM_001018005.1, *TRDN*-NM_006073.2, *TRPM4*-NM_017636.3, *TTN*-NM_003319.4, *TTR*-NM_000371.3, *TXNRD2*-NM_006440.3, *VCL*-NM_014000.2.

Analytical range: This test detects variants in the coding domains and well into the flanking 5' and 3' ends of the introns and untranslated regions. Unless explicitly stated, sequence and copy number variants in the promoter, non-coding exons, or 3' untranslated regions are not routinely reported.

Analytical range exceptions:

- **ALPK3:** only full gene deletion/duplications are routinely reported.
- **ANK2:** variants in the brain-specific exon 38 are not reported.
- **FLNC:** sequence variations of exons 46-48 are not analyzed or reported. Only full gene deletion/duplications are routinely reported.
- **TTN:** only truncating variants are routinely reported.
- **Gross deletion/duplication analysis is not performed for the following genes:** *ALMS1*, *CALM2*, *CALM3*, *DOLK*, *FHL1*, *RIT1*, *SCN10A*, *SOS1*, and *TECRL*.

Reporting: Results reported herein may be of constitutional or somatic origin. This methodology cannot differentiate between these possibilities. In result reports, variants in the following classifications are always reported, and are based on the following definitions and clinical recommendations:

- **Pathogenic Variant:** variants with sufficient evidence to classify as pathogenic (capable of causing disease). Targeted testing of at-risk relatives and appropriate changes in medical management for pathogenic variant carriers recommended. Previously described pathogenic variants, including intronic variants at any position, are always reported when detected.
- **Variant, Likely Pathogenic (VLP):** variants with strong evidence in favor of pathogenicity. Targeted testing of at-risk relatives and appropriate changes in medical management for VLP carriers typically recommended. Previously described likely pathogenic variants, including intronic VLPs at any position, are always reported when detected.
- **Variant, Uncertain Significance (VUS):** variants with limited and/or conflicting evidence regarding pathogenicity. Familial testing via the Family Studies Program may be recommended. Medical management to be based on personal/family clinical histories, not VUS carrier status. Note, intronic VUSs are always reported out to 5 base pairs from the splice junction when detected.

Variants of unlikely clinical significance (those with strong/very strong evidence to argue against pathogenicity) are not routinely included in results. These include findings classified as "likely benign" and "benign" variants. Classification and interpretation of variants may change over time with accumulating evidence and scientific advancements. Updated classifications may be reported through reclassification notices; however, clients should re-contact the laboratory or visit ClinVar (<https://www.ncbi.nlm.nih.gov/clinvar/>) for the most up to date information regarding the current interpretation of results.

All results, including those from prior genetic testing for themselves and/or family members, will be reported as described above.

Gender identity (if provided) is not used in the interpretation of results, and sex assigned at birth is used in the interpretation of results only when

necessary. Currently, there are insufficient data to determine specific risk adjustments for transgender, nonbinary, or intersex individuals.

Assay Information Continued on Next Page

ASSAY INFORMATION (Supplement to Test Results - Continued)

Resources: The following references are used in variant analysis and classification when applicable for observed genetic alterations.

1. The 1000 Genomes Project Consortium. An integrated map of genetic variation from 1092 human genomes. *Nature*. 2012;491:56-65.
2. ACMG Standards and guidelines for the interpretation of sequence variants. *Genet Med*. 2015 May;17(5):405-23.
3. Ambry Genetics Variant Classification Scheme. <http://www.ambrygen.com/variant-classification>.
4. Berkeley Drosophila Genome Project [Internet]. Reese MG et al. *J Comp Biol*. 1997;4:311-23. http://www.fruitfly.org/seq_tools/splice.html.
5. Database of Single Nucleotide Polymorphisms (dbSNP) [Internet]. Bethesda (MD): National Center for Biotechnology Information, National Library of Medicine (dbSNP Build ID:135) Available from: www.ncbi.nlm.nih.gov/SNP. Accessed Jan 2012).
6. ESEfinder [Internet]. Smith PJ, et al. (2006) *Hum Mol Genet*. 15(16):2490-2508 and Cartegni L, et al. *Nucleic Acid Research*. 2003;31(13):3568-3571. <http://rulai.cshl.edu/cgi-bin/tools/ESE3/esefinder.cgi?process=home>.
7. Exome Variant Server, NHLBI Exome Sequencing Project (ESP) [Internet], Seattle WA. Available from: evs.gs.washington.edu/EVS.
8. Grantham R. Amino acid difference formula to help explain protein evolution. *Science*. 1974;185(4151):862-864.
9. HGMD® [Internet]. Stenson PD et al. *Genome Med*. 2009;1(1):13. www.hgmd.cf.ac.uk.
10. Landrum MJ et al. ClinVar: public archive of relationships among sequence variation and human phenotype. *Nucleic Acids Res*. 2014 Jan 1;42(1):D980-5. doi: 10.1093/nar/gkt1113. PubMed PMID: 24234437.
11. Online Mendelian Inheritance in Man, OMIM®. McKusick-Nathans Institute of Genetic Medicine, Johns Hopkins University (Baltimore, MD), Copyright® 1966-2012. World Wide Web URL: <http://omim.org>.
12. Feng BJ. PERCH: A Unified Framework for Disease Gene Prioritization. *Hum Mutat*. 2017 Mar;38(3):243-251.
13. Exome Aggregation Consortium (ExAC) [Internet], Cambridge, MA. Available from: <http://exac.broadinstitute.org>.
14. Genome Aggregation Database (gnomAD) [Internet], Cambridge, MA. Available from: <http://gnomad.broadinstitute.org>.
15. Lek M et al. Analysis of protein-coding genetic variation in 60,706 humans. *Nature*. 2016 Aug 17;536(7616):285-91. PMID: 27535533
16. Mu W et al. *J Mol Diagn*. 2016 Oct 4. PubMed PMID: 27720647
17. Karczewski KJ et al. *Nature*. 2020 May;581(7809):434-443. PMID: 32461654
18. Splicing Prediction: Jaganathan K et al. *Cell*. 2019 Jan 24; 176(3):535-548.e24. PMID: 30661751

Disclaimer: This test was developed, and its performance characteristics were determined by Ambry Genetics Corporation. It has not been cleared or approved by the US Food and Drug Administration (FDA). The FDA does not require this test to go through premarket FDA review. It should not be regarded as investigational or for research. This test should be interpreted in context with other clinical findings. This report does not represent medical advice. Any questions, suggestions, or concerns regarding interpretation of results should be forwarded to a genetic counselor, medical geneticist, or physician skilled in interpretation of the relevant medical literature. This laboratory is certified under the Clinical Laboratory Improvement Amendments (CLIA) as qualified to perform high complexity clinical laboratory testing. This test analyzes the following types of mutations: nucleotide substitutions, small deletions (up to 25 bp), small insertions (up to 10 bp), small indels, and gross deletions/duplications. Unless otherwise noted in the methodology section above, this test is not intended to analyze the following types of alterations: gross rearrangements, deep intronic variations, mobile element insertions, and other unknown abnormalities. The pattern of mutation types varies by gene, and this test detects a high but variable percentage of known and unknown mutations of the classes stated. A negative result from the analysis cannot rule out the possibility that the tested individual carries a rare unexamined mutation or mutation in the undetectable group. This test is designed and validated to be capable of detecting ~99.9% of described mutations in the genes represented on the test, listed above (analytical sensitivity). The clinical sensitivity of this test may vary widely according to the specific clinical and family history. Mutations in other genes or the regions not analyzed by this test can also give rise to similar clinical conditions. Although molecular tests are highly accurate, rare diagnostic errors may occur. Possible diagnostic errors include sample mix-up, erroneous paternity identification, technical errors, clerical errors, and genotyping errors. Genotyping errors can result from trace contamination of PCR reactions, from maternal cell contamination in fetal samples, from rare genetic variants that interfere with analysis, germline or somatic mosaicism, presence of pseudogenes, technical difficulties in regions with high GC content or homopolymer tracts, active hematologic disease, a history of allogeneic bone marrow or peripheral stem cell transplant, or from other sources. Rare variants present in the human genome reference sequence (GRCh37.p5/hg19) or rare misalignment due to presence of pseudogenes can lead to misinterpretation of patient sequence data.

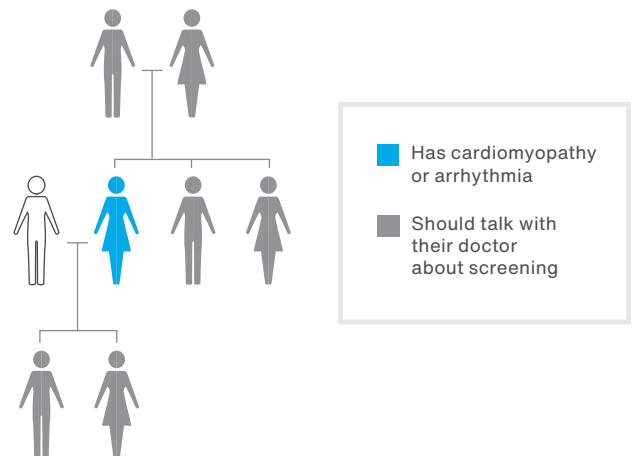
Understanding Your Negative Cardiovascular Genetic Test Result

INFORMATION FOR PATIENTS

Result	NEGATIVE	Your testing did not find any gene changes (mutations) that cause cardiovascular disease. Not all patients with inherited cardiovascular disorders have a mutation in a gene in this test. You may have a mutation in a gene that was not included in this test. If someone in your family has a specific mutation in one of the genes in this test, it is likely that you do not carry that mutation.
Diagnosis	NO CHANGE	This testing does not change your cardiovascular diagnosis. If you have been diagnosed with cardiomyopathy, arrhythmia, or another cardiovascular disorder, that remains the same.
Further Testing	DISCUSS	More genetic testing may be right for you. Please talk about this with your doctor or genetic counselor.
Management Options	PATIENTS WITH ARRHYTHMIA OR CARDIOMYOPATHY	Treatment options include: medications, surgery, pacemakers, implantable cardioverter defibrillators (ICDs), or avoiding certain athletic activities. Talk to your doctor about which may be right for you.
Screening Options	PATIENTS WITH A FAMILY HISTORY OF CARDIOMYOPATHY OR ARRHYTHMIA BUT NO PERSONAL SIGNS	Options for screening and early detection include: physical exams, echocardiograms, electrocardiograms (EKGs), or cardiac MRI. Talk to your doctor about whether these options are right for you.
Next Steps	DISCUSS	Please share this with family members so they can talk with their doctors and learn more.
Reach Out	RESOURCES	<ul style="list-style-type: none"> • Ambry’s Cardiology Site for Families patients.ambrygen.com/cardiology • National Society of Genetic Counselors nsgc.org • Hypertrophic Cardiomyopathy Association 4hcm.org • Sudden Arrhythmia Death Syndromes (SADS) Foundation sads.org • Genetic Information Nondiscrimination Act (GINA) ginahelp.org

Cardiomyopathy or Arrhythmia in the Family

Even though your genetic testing was negative, some cardiomyopathies and arrhythmias can run in families. All close family members of someone with an inherited cardiomyopathy or arrhythmia (like parents, brothers, sisters, children) should talk with their doctor about screening.



Please discuss this information with your healthcare provider. The field of genetics is continuously changing, so updates related to your result, medical recommendations, and/or potential treatments may be available over time. This information is not meant to replace a discussion with a healthcare provider, and should not be considered or taken as medical advice.