MAYO CLINIC LABORATORIES

NEW TEST

Notification Date: October 20, 2023
Effective Date: October 26, 2023

Postmortem Cardiomyopathy and Arrhythmia Gene Panel, Tissue

Test ID: PMCAG

Useful for:

- Providing a comprehensive postmortem genetic evaluation in the setting of a sudden death attributed to cardiomyopathy or suspicious for cardiac arrhythmia or with a personal or family history suggestive of a hereditary form of cardiomyopathy or cardiac arrhythmia
- Identifying a disease-causing variant in the decedent, which may assist with risk assessment and predictive testing of at-risk family members

Genetics Information:

- This test utilizes next-generation sequencing to detect single nucleotide variants and deletions-insertions (delins) in 105 genes associated with hereditary forms of cardiomyopathy and cardiac arrhythmia: *ABCC9, ACAD9, ACADVL, ACTC1, ACTN2, AGL, ALMS1, ALPK3, ANK2, BAG3, BRAF, CACNA1C, CACNA1D, CACNA2D1, CACNB2, CALM1, CALM2 , CALM3, CASQ2, CAV3, CDH2, CPT2, CRYAB, CSRP3, DES, DMD, DNAJC19, DOLK, DSC2, DSG2, DSP, ELAC2, EMD, FHL1, FKRP, FKTN, FLNC, GAA, GLA, GNB5, HCN4, HRAS, JPH2, JUP, KCND2, KCND3, KCNE1, KCNE2, KCNH2, KCNJ2, KCNJ8, KCNQ1, KRAS, LAMP2, LMNA, LZTR1, MAP2K1, MAP2K2, MRAS, MTO1, MYBPC3, MYH7, MYL2, MYL3, MYLK3, MYPN, NEXN, NKX2-5, NRAS, PCCA, PCCB, PKP2, PLN, PPA2, PPCS, PRDM16, PRKAG2, PTPN11, RAF1, RBM20, RIT1, RYR2, SCN5A, SGCD, SHOC2, SLC22A5, SLC4A3, SOS1, SOS2, TAZ (TAFAZZIN), TBX20, TCAP, TECRL, TMEM43, TMEM70, TNNC1, TNNI3, TNNI3K, TNNT2, TPM1, TRDN, TRIM63, TTN, TTR,* and *VCL*.
- Identification of a disease-causing variant may assist with familial risk assessment, screening, and genetic counseling for cardiomyopathy and cardiac arrhythmia.

Ordering Guidance:

- This test is intended for use when whole blood is not available and formalin-fixed, paraffin-embedded (FFPE) tissue is the only available specimen. If whole blood is available, consider CACMG / Comprehensive Arrhythmia and Cardiomyopathy Gene Panel, Varies.
- Targeted testing for familial variants (also called site-specific or known variants testing) is available for the genes on this panel. See FMTT / Familial Mutation, Targeted Testing, Varies. To obtain more information about this testing option, call 800-533-1710.

Methods:

Sequence Capture and Targeted Next-Generation Sequencing (NGS)

Reference Values:

An interpretive report will be provided.

Specimen Requirements:

Specimen Type: Tissue block

Collection Instructions: Submit a formalin-fixed, paraffin-embedded tissue block

Additional Information: Testing will be attempted on blocks of any age but may be canceled if adequate DNA concentration cannot be obtained.

Specimen Stability Information:

Specimen Type	Temperature	Time	Special Container
Varies	Ambient (preferred)		
	Refrigerated		

Cautions:

Clinical Correlations:

- Test results should be interpreted in the context of clinical findings, family history, and other laboratory data. Misinterpretation of results may occur if the information provided is inaccurate or incomplete.
- 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 in an affected family member would allow for more informative testing of at-risk individuals.
- To discuss the availability of additional testing options or for assistance in the interpretation of these results, contact Mayo Clinic Laboratories genetic counselors at 800-533-1710.

Technical Limitations:

- Next-generation sequencing (NGS) 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; assay performance below the minimum acceptable criteria or for failed regions will be noted. 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 evaluated by sequencing as a result of technical limitations of the assay, including regions of homology, high guanine-cytosine (GC) content, and repetitive sequences. Confirmation of NGS results by Sanger sequencing is typically not performed for this test.
- Deletions-insertions (delins) of 40 or more base pairs, including mobile element insertions, may be less reliably detected than smaller delins.
- Deletion/duplication analysis is not performed due to technical limitations of the formalin-fixed paraffin-embedded specimen type.
- This test is not designed to detect low levels of mosaicism or 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.
- Genes may be added or removed based on updated clinical relevance. For detailed information regarding gene-specific performance and technical limitations, see Method Description or contact a laboratory genetic counselor.

Reclassification of Variants:

- Currently, it is not standard practice for the laboratory to systematically review previously classified variants on a regular basis. The laboratory encourages healthcare providers to contact the laboratory at any time to learn how the classification of a particular variant may have changed over time. Due to broadening genetic

knowledge, it is possible that the laboratory may discover new information of relevance to the patient. Should that occur, the laboratory may issue an amended report.

Variant Evaluation:

- Evaluation and categorization of variants are performed using published American College of Medical Genetics and Genomics and the Association for Molecular Pathology recommendations as a guideline. Other gene-specific guidelines may also be considered. Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance. Variants classified as benign or likely benign are not reported.
- Multiple in silico evaluation tools may be used to assist in the interpretation of these results. The accuracy of predictions made by in silico evaluation tools is highly dependent upon the data available for a given gene, and periodic updates to these tools may cause predictions to change over time. Results from in silico evaluation tools should be interpreted with caution and professional clinical judgment.
- Rarely, incidental or secondary findings may implicate another predisposition or presence of active disease. Incidental findings may include, but are not limited to, results related to the sex chromosomes. These findings will be carefully reviewed to determine whether they will be reported.

CPT Code:

81439

Day(s) Performed: Varies

Report Available: 28 to 42 days

Questions

Contact Michelle Raths, Laboratory Resource Coordinator at 800-533-1710.