Cardiovascular Panel Testing

CARDIOVASCULAR PANELS

Six different gene panels are available based on clinical indication. Please refer to the individual panels for gene content and detailed information.

- **Cardiomyopathy, Arrhythmia and Sudden Death Panel** (127 genes)
  - (EPIC Order code=LAB17037) (CPT code=81479)
- **Cardiomyopathy Panel** (106 genes)
  - (EPIC Order code=LAB17076) (CPT code=81439)
- **Arrhythmia Panel** (59 genes)
  - (EPIC Order code=LAB17077) (CPT code=81413)
- **Pulmonary Hypertension Panel** (14 genes)
  - (EPIC Order code: LAB17039) (CPT code=81479)
- **Aortopathy and FTAAD Panel** (35 genes)
  - (EPIC Order code=LAB17038) (CPT code=81410)
- **Familial Hypercholesterolemia Panel** (36 genes)
  - (EPIC Order code=LAB11335) (CPT code=81479)

The healthcare provider is also required to complete and submit a **Consent Form**.

- This can be found on the INFONET. Search for “Hereditary Cardiovascular Genetic Testing Acknowledgement Form.”
- If EPIC is not an option, please complete and submit a paper requisition to GenomicsLab@upmc.edu.

BACKGROUND

Individuals with disorders related to lipid metabolism, thoracic aortic disease, pulmonary hypertension, cardiomyopathies, and arrhythmic disorders are particularly likely to have a heritable cause, especially if there is also a family history of these conditions. Individuals identified to have likely pathogenic and/or pathogenic variant(s) have increased lifetime risks of developing cardiovascular disease.

This information may assist with diagnosis, prognosis, treatment, reproductive planning, familial screening, and genetic counseling. The identification of a pathogenic variant can inform targeted management strategies and personalized therapies for affected patients, enhanced surveillance and/or preventive care for unaffected patients, and predictive testing and risk assessment for at-risk blood relatives.

INDICATIONS FOR TESTING

- Personal history of a confirmed or suspected heritable cardiovascular disease

RESULTS

Positive: A pathogenic or likely pathogenic variant(s) was detected, which would either explain the patient’s symptoms or increase the risk of developing certain types of cardiovascular conditions. The healthcare provider can use the result to guide the patient’s medical management. Family members can be tested for the variant to determine their cardiovascular disease and/or reproductive risk.

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Negative: No clinically significant variants were detected in the gene panel. This does not rule out the possibility of variants in other genes or variants that are not detectable in this assay. Cardiovascular disease risk may still be increased based on the family history. The healthcare provider will discuss these risks and develop a screening plan based on the patient's personal risk factors. The healthcare provider may also discuss more testing, either now or in the future.

Variant of Uncertain Significance (VUS): A variant was detected; however, it is uncertain whether this variant is the cause of a patient's symptoms since current information about the variant is limited. The result is not clinically actionable. Screening should be based on personal and family history.

METHOD

Targeted panel sequencing was carried out using a genome sequencing backbone to enable comprehensive capture, with analysis restricted to the exonic regions of the genes included in this panel. Genomic DNA is fragmented, adaptors are ligated to the fragment ends, and libraries are sequenced on Illumina next generation sequencing (NGS) systems using 2×150 bp paired-end reads at the High Throughput Genomics Core. The average mean sequencing coverage across the nuclear genome is at least 30X. Bi-directional sequence reads are assembled and aligned to the GRCh38 human genome reference. Sequencing variants including single nucleotide substitutions (SNVs), small deletions, small insertions, small indels, and copy number variants (CNVs) are detected using the Illumina DRAGEN Bio-IT Platform. Variants are called at a minimum of 8X coverage and a variant allele fraction of ≥20%. Variants are annotated using commercially available software and are interpreted and classified according to ACMG/AMP standards and guidelines. Reportable variants that do not meet laboratory quality criteria are confirmed using Sanger sequencing, ddPCR, long-range PCR, breakpoint PCR, MLPA, or another validated method prior to reporting. Variants classified as likely benign or benign are not confirmed or reported.

LIMITATIONS

This assay is designed to detect single nucleotide substitutions (SNVs), small deletions (≤20 bp), small insertions (≤10 bp), small indels, and copy number variants (CNVs) greater than 1 kb in size. Although a genome sequencing backbone was used, variants outside the targeted exonic regions of the panel genes (see GENES EVALUATED) were not analyzed or reported. Some genomic regions have inherent complex sequence features such as homology, pseudogene content, or high GC composition that may yield suboptimal data and increase the likelihood of missed variants across variant types. Detection of CNVs smaller than 1 kb is limited and not validated for routine clinical reporting; however, potential sub-kilobase CNV findings may be further evaluated at the discretion of the laboratory director. CNV detection sensitivity may be reduced in regions with variable coverage, poor mappability, high GC content, or repetitive sequences. CNV analysis does not detect balanced chromosomal alterations including reciprocal or Robertsonian translocations, balanced inversions, or complex genomic rearrangements. This test does not detect methylation abnormalities. This test does not detect methylation abnormalities. The assay is not specifically designed to detect mosaicism; however, potential mosaic findings may be further evaluated at the discretion of the laboratory director. Although molecular tests are highly accurate, rare diagnostic errors may occur.

The classification and interpretation of all variants identified in this assay reflect the current state of the laboratory's scientific understanding at the time this report was issued. Variant classification and interpretation may change for a variety of reasons, including, but not limited to, improvements to classification techniques, availability of additional scientific information and observation of a variant in more patients.

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SPECIMEN REQUIREMENTS

- Whole blood – EDTA tube required, 3-5 ml
- Previously extracted DNA (concentration >14.3 ng/ul, volume >20 ul, minimum of 2 µg gDNA from Blood; 1.1 µg gDNA from saliva)
- Saliva provided in Oragene (OGD-500) collection kits accepted for relatives only

TURNAROUND TIME

Four weeks post complete order date, defined as the date when insurance authorization is obtained or the patient's out-of-pocket (OOP) cost is approved.

CPT CODE

Refer to specific gene panel