Heart disease is listed by the CDC as the leading cause of death. Many cardiac diseases have multifactorial causes, but research indicates that genetic predispositions frequently play an important etiological role. Cardiac diseases that affect the heart muscle are referred to as cardiomyopathies. Dilated cardiomyopathies are characterized by an enlargement and weakening of the ventricles that leads to a progressive enlargement of the heart and impairment of the systolic pump functions. Weakening of the heart muscle eventually leads to heart failure and is the most common reason why dilated cardiomyopathy patients are referred for cardiac transplantation. It is estimated that in the United States about 750,000 people have dilated cardiomyopathy; of these about one third can be classified as familial.

Familial dilated cardiomyopathies, caused by a mutation in a single gene or in more than one gene, may be associated with several different clinical presentations; however, mutations in different genes may also attribute to similar phenotypes. Next-Generation Sequencing facilitates analysis of multiple genes at the same time and thereby increases the likelihood of detecting potentially pathogenic mutations that may predispose an individual to develop a dilated cardiomyopathy.

**Indications for Testing**

1. Molecular confirmation of a clinical diagnosis of hereditary dilated cardiomyopathy (DCM) in symptomatic patients.
2. Assessment for at-risk family members
3. Carrier testing of asymptomatic family members of an affected proband

**Requisition Form:** Cardiac Test Requisition Form or General Test Requisition Form ([www.apollogen.com](http://www.apollogen.com))

**Genes (33):** ABCC9, ACTC1, ACTN2, DES, LAMA4, LDB3, LMNA, MT-TH, MT-TI, MT-TK, MT-TL1, MT-TL2, MT-TM, MT-TQ, MT-TS1, MT-TS2, MYBPC3, MYH6, MYH7, MYPN, PLN, PSEN1, PSEN2, RBM20, SCN5A, SGCD, TAZ, TCAP, TMPO, TNNI3, TNNT2, TPM1, and VCL

**CPT Codes:** 81401x2, 81403x2; 81405x6, 81406x5, 81407x4, 81479x14
**Turnaround Time:** 4 weeks

**Specimen Requirement:** 3-5 mL Blood (EDTA) – Lavender Top Tube (preferred); Saliva samples are optional

**Other Specimen Types:** Contact ApolloGen Diagnostic Laboratory

**Pricing:** Please contact us at (949) 916-8886 or at inquiries@apollogen.com for current pricing

**Testing Methodology**

Genomic DNA is extracted from the patient’s specimen and fragmented via sonication. All of the exons, flanking intronic (at least 10 nucleotides into the introns), and untranslated regions (5’ and 3’) of the
targeted genes are enriched using capture-based hybridization. Massively parallel sequencing is applied to the enriched target DNA regions to detect mutation. The region <10-fold coverage is regarded as a low coverage region and will be rescued by Sanger Sequencing. Variants with an allele frequency > 1% are considered likely benign polymorphisms, and are not included in the final report. Interpretation of rare alterations with allele frequency <1% is based on ACMG guidelines. All pathogenic and likely pathogenic variants are verified by Sanger Sequencing.

Massively parallel sequencing can reliably detect insertion/deletion mutations smaller than 10 base pairs. However, larger insertion, deletion, duplication due to rearrangement, and mutations in regulatory and deep intronic regions cannot be detected by this technology. Rare primer site variants may lead to erroneous results that may need further investigation.

**Analytical Sensitivity:**
This test can detect >95% of the small variants in the examined regions. Please contact us for detailed information regarding coverage for specific genes of interest.

**Related Tests**

**Hypertrophic Cardiomyopathy Panel**
Analyzes 18 critical genes that have been associated with hypertrophic cardiomyopathy

**Comprehensive Cardiomyopathy Panel**
Simultaneously analyzes 44 critical genes associated with an increased risk for cardiomyopathies and other cardiac disorders.

**Variant Classification**
Sequencing results will be interpreted and reported following the recommendations of the American College of Medical Genetics ([www.acmg.net](http://www.acmg.net)). Sequence variations will be analyzed and classified into the following categories based on current scientific knowledge. Variants found in categories 1-3 (pathogenic, likely pathogenic, and variants of unknown clinical significance) will be reported.

1. **Pathogenic:** Pathogenic variants include nonsense mutations and frame shift mutations that are predicted to result in premature protein truncation, splice site mutations, and previously reported missense mutations that are recognized as disease-causing by databases and the scientific literature.
2. **Likely Pathogenic:** Likely pathogenic variants are those variants that are likely to adversely affect gene function, but for which there is no conclusive evidence to strongly support pathogenicity.
3. **Variant of Unknown Clinical Significance (VUS):** VUSs are sequence variations for which there is insufficient evidence to either confirm or exclude pathogenicity.
4. **Likely Benign:** Likely benign variants are sequence variations for which there is significant, but not conclusive evidence supporting that the variant is not disease-causing.
5. **Negative:** A negative classification is reported when no disease-causing variant is found, or a variant is classified as a benign polymorphism based on the population data, or if there is no clinical significance based on review of the literature and mutation databases.

**References**


