Overview

Useful For

Providing a comprehensive genetic evaluation for patients with a personal or family history suggestive of hereditary dilated cardiomyopathy (DCM)

Establishing a diagnosis of a hereditary DCM, and in some cases, allowing for appropriate management and surveillance for disease features based on the gene involved

Identifying a pathogenic variant within a gene known to be associated with disease features that allows for predictive testing of at-risk family members

Genetics Test Information

This test uses next generation sequencing to test for variants in the ABCC9, ACTC1, ACTN2, ANKRD1, CRYAB, CSRP3, DES, LAMA4, LAMP2, LDB3, LMNA, MYBPC3, MYH6, MYH7, MYPN, NEXN, PLN, RAF1, RBM20, SCN5A, SGCD, TAZ, TCAP, TNNC1, TNNI3, TNNT2, TPM1, TTN (excluding the following genomic regions: Chr2(GRCh37):g. 179523879-179524002 and Chr2(GRCh37):g. 179523712-179523835), TTR, and VCL genes.

This test uses Sanger sequencing to test for variants in certain exons of the following genes:

- MYH6 exon 26
- MYH7 exon 27

Identification of a pathogenic variant may assist with prognosis, clinical management, familial screening, and genetic counseling.

Prior Authorization is available for this assay; see Special Instructions.

Special Instructions

- Informed Consent for Genetic Testing
- Dilated Cardiomyopathy Multi-Gene Panel Prior Authorization Ordering Instructions
- Hereditary Cardiomyopathies and Arrhythmias: Patient Information
- Informed Consent for Genetic Testing (Spanish)

Method Name

Custom Sequence Capture and Targeted Next-Generation Sequencing followed by Polymerase Chain Reaction (PCR) and supplemental Sanger Sequencing

NY State Available

Yes

Specimen

Specimen Type

Whole Blood EDTA

Advisory Information

Targeted testing for familial variants (also called site-specific or known mutation testing) is available for the genes on
Test Definition: DCMGP
Dilated Cardiomyopathy Panel, B

this panel. See:

- KVAR1 / Known Variant Analysis-1 Variant, Varies
- KVAR2 / Known Variant Analysis-2 Variants, Varies
- KVAR3 / Known Variant Analysis-3+ Variants, Varies

Call 800-533-1710 to confirm the appropriate test for targeted testing.

Necessary Information

1. Hereditary Cardiomyopathies and Arrhythmias: Patient Information (T725) is required, see Special Instructions. Testing may proceed without the patient information however it aids in providing a more thorough interpretation. Ordering providers are strongly encouraged to complete the form and send it with the specimen.

2. Include physician name and phone number with specimen.

Specimen Required

Container/Tube: Lavender top (EDTA)

Specimen Volume: 3 mL

Collection Instructions: Send specimen in original tube.

Additional Information: Prior Authorization is available for this test. Submit the required form with the specimen.

Forms

1. New York Clients-Informed consent is required. Document on the request form or electronic order that a copy is on file. The following documents are available in Special Instructions:

   - Informed Consent for Genetic Testing (T576)
   - Informed Consent for Genetic Testing (Spanish) (T826)

2. Dilated Cardiomyopathy Multi-Gene Panel Prior Authorization Ordering Instructions in Special Instruction

3. If not ordering electronically, complete, print, and send a Cardiovascular Test Request Form (T724) with the specimen.

Specimen Minimum Volume

1 mL

Reject Due To

All specimens will be evaluated by Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
<th>Special Container</th>
</tr>
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<tbody>
<tr>
<td>Whole Blood EDTA</td>
<td>Ambient (preferred)</td>
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</tr>
<tr>
<td></td>
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Clinical and Interpretive

Clinical Information

The cardiomyopathies are a group of disorders characterized by disease of the heart muscle. Cardiomyopathy can be caused by inherited, genetic factors, or by nongenetic (acquired) causes such as infection or trauma. When the presence or severity of the cardiomyopathy observed in a patient cannot be explained by acquired causes, genetic testing for the inherited forms of cardiomyopathy may be considered. Overall, the cardiomyopathies are some of the most common genetic disorders. The inherited forms of cardiomyopathy include hypertrophic cardiomyopathy (HCM), dilated cardiomyopathy (DCM), arrhythmogenic right ventricular cardiomyopathy (ARVC), and left ventricular noncompaction (LVNC).

DCM is established by the presence of left ventricular enlargement and systolic dysfunction. DCM may present with heart failure with symptoms of congestion, arrhythmias, and conduction system disease, or thromboembolic disease (stroke). The most recent estimates of the incidence of DCM suggest that the condition affects approximately 1 in every 250 people. These estimates are higher than originally reported due to subclinical phenotypes and underdiagnosis. After exclusion of nongenetic causes such as ischemic injury, DCM is traditionally referred to as "idiopathic" dilated cardiomyopathy. Approximately 20% to 50% of individuals with idiopathic DCM may have an identifiable genetic cause for their disease. Families with 2 or more affected individuals are diagnosed with familial dilated cardiomyopathy.

The majority of familial dilated cardiomyopathy is inherited in an autosomal dominant manner; however, autosomal recessive and X-linked forms have also been reported. At least 28 genes have been reported in association with DCM, including genes encoding the cardiac sarcomere and other proteins involved in proteins responsible for cardiac muscle contraction. Some genes associated with DCM also cause other forms of hereditary cardiomyopathy, cardiac channelopathies, skeletal myopathies, or metabolic defects. See table for details regarding the genes tested by this panel and associated diseases.

Genes included in the Dilated Cardiomyopathy Multi-Gene Panel

<table>
<thead>
<tr>
<th>Gene</th>
<th>Protein</th>
<th>Inheritance</th>
<th>Disease Association</th>
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<tbody>
<tr>
<td>ABCC9</td>
<td>ATP-Binding cassette, subfamily C, member 9</td>
<td>AD</td>
<td>DCM, Cantu syndrome</td>
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<tr>
<td>ACTC1</td>
<td>Actin, alpha, cardiac muscle</td>
<td>AD</td>
<td>CHD, DCM, HCM, LVNC</td>
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<td>ACTN2</td>
<td>Actinin, alpha-2</td>
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<td>ANKRD1</td>
<td>Ankyrin repeat domain-containing protein 1</td>
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<td>CRYAB</td>
<td>Crystallin, alpha-B</td>
<td>AD, AR</td>
<td>DCM, myofibrillar myopathy</td>
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<td>CSRP3</td>
<td>Cysteine-and glycine-rich protein 3</td>
<td>AD</td>
<td>HCM, DCM</td>
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<td>Gene</td>
<td>Description</td>
<td>Inheritance</td>
<td>Conditions</td>
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<tr>
<td>DES</td>
<td>Desmin</td>
<td>AD, AR</td>
<td>DCM, ARVC, myofibrillar myopathy, RCM with AV block, neurogenic scapuloperoneal syndrome Kaeser type, LGMD</td>
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<td>LAMA4</td>
<td>Laminin, alpha-4</td>
<td>AD</td>
<td>DCM</td>
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<td>LAMP2</td>
<td>Lysosome-associated membrane protein 2</td>
<td>X-linked</td>
<td>Danon disease</td>
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<td>LDB3</td>
<td>LIM domain-binding 3</td>
<td>AD</td>
<td>DCM, LVNC, myofibrillar myopathy</td>
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<td>LMNA</td>
<td>Lamin A/C</td>
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<td>DCM, EMD, LGMD, congenital muscular dystrophy (see OMIM for full listing)</td>
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<td>Myosin-binding protein-C, cardiac</td>
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<td>Myosin, heavy chain 6, cardiac muscle, alpha</td>
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<td>Phospholamban</td>
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<td>RAF1</td>
<td>V-raf-1 murine leukemia viral oncogene homolog 1</td>
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<td>RNA-binding motif protein 20</td>
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<td>DCM</td>
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<td>SCN5A</td>
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<td>Brugada syndrome, DCM, Heart block, LQTS, SSS, SIDS</td>
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<td>TAZ</td>
<td>Tafazzin</td>
<td>X-linked</td>
<td>Barth syndrome, LVNC, DCM</td>
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<td>Troponin C, slow</td>
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<td>TNNI3</td>
<td>Troponin I, cardiac</td>
<td>AD, AR</td>
<td>DCM, HCM, RCM</td>
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<td>TNNT2</td>
<td>Troponin T2, cardiac</td>
<td>AD</td>
<td>HCM, DCM, RCM, LVNC</td>
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<td>TPM1</td>
<td>Tropomyosin 1</td>
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<td>Titin</td>
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<td>HCM, DCM, ARVC myopathy</td>
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<td>Transthyretin</td>
<td>AD</td>
<td>Transthyretin-related amyloidosis</td>
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Test Definition: DCMGP
Dilated Cardiomyopathy Panel, B

| VCL | Vinculin | AD | HCM, DCM |

Abbreviations: Hypertrophic cardiomyopathy (HCM), dilated cardiomyopathy (DCM), arrhythmogenic right ventricular cardiomyopathy (ARVC), left ventricular noncompaction cardiomyopathy (LVNC), restrictive cardiomyopathy (RCM), limb-girdle muscular dystrophy (LGMD), Emory muscular dystrophy (EMD), congenital heart defects (CHD), sudden infant death syndrome (SIDS), long QT syndrome (LQTS), sick sinus syndrome (SSS), autosomal dominant (AD), autosomal recessive (AR)

Reference Values
An interpretive report will be provided.

Interpretation
Evaluation and categorization of variants is performed using the most recent published American College of Medical Genetics and Genomics (ACMG) recommendations as a guideline. Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance.

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 predictions made by these tools may change over time. Results from in silico evaluation tools should be interpreted with caution and professional clinical judgment.

Cautions
Clinical Correlations:

Some individuals who have involvement of 1 or more of the genes on the panel may have a variant that is not identified by the methods performed (eg, promoter variants, deep intronic variants). The absence of a variant, therefore, does not eliminate the possibility of a hereditary dilated cardiomyopathy (DMC) or a related disorder.

Test results should be interpreted in 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 family history of hereditary DMC or a related disorder, it is often useful to first test an affected family member. Identification of a pathogenic variant in an affected individual allows for more informative testing of at-risk individuals.

Technical Limitations:

Next-generation sequencing may not detect all types of genetic variants. Additionally, rare polymorphisms may be present that could lead to false-negative or false-positive results. If results do not match clinical findings, consider alternative methods for analyzing these genes, such as Sanger sequencing or large deletion/duplication analysis. If the patient has had an allogeneic blood or marrow transplant or a recent (ie, less than 6 weeks from time of sample collection) heterologous blood transfusion, results may be inaccurate due to the presence of donor DNA.

Reclassification of Variants Policy:

At this time, it is not standard practice for the laboratory to systematically review likely pathogenic variants or variants of uncertain significance that are detected and reported. The laboratory encourages health care providers to contact the laboratory at any time to learn how the status of a particular variant may have changed over time. Consultation
with a genetics professional should be considered for interpretation of this result.

A list of benign and likely benign variants detected for this patient is available from the laboratory upon request.

Contact the laboratory if additional information is required regarding the transcript or human genome assembly used for the analysis of this patient's results.

**Clinical Reference**


**Performance**

**Method Description**

Next-generation sequencing (NGS) is performed using an Illumina instrument with paired-end reads. The DNA is prepared for NGS using a custom Agilent SureSelect Target Enrichment System. Data is analyzed with a bioinformatics software pipeline. Supplemental and/or confirmatory Sanger sequencing is performed when necessary.(Unpublished Mayo method)

The following genes are evaluated in this multigene panel: **ABCC9, ACTC1, ACTN2, ANKR1, CRYAB, CSRP3, DES, LAMA4, LAMP2, LDB3, LMNA, MYBPC3, MYH6, MYH7, MYPN, NEXN, PLN, RAF1, RBM20, SCN5A, SGCD, TAZ, TCAP, TNRC1, TNNT2, TPM1, TTN** (excluding the following genomic regions: Chr2(GRCh37):g. 179523879-179524002 and Chr2(GRCh37):g. 179523712-179523835), **TTR**, and **VCL**.

**PDF Report**

No

**Day(s) and Time(s) Test Performed**

Wednesday; Varies

**Analytic Time**

4 weeks after prior authorization approved
Test Definition: DCMGP
Dilated Cardiomyopathy Panel, B

Maximum Laboratory Time
6 weeks

Specimen Retention Time
Extracted DNA: 2 months

Performing Laboratory Location
Rochester

Fees and Codes

Fees
- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact Customer Service.

Test Classification
This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.

CPT Code Information
81439

LOINC® Information

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<th>Test Order Name</th>
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<td>DCMGP</td>
<td>Dilated Cardiomyopathy Panel, B</td>
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Prior Authorization
Insurance preauthorization is available for this testing; forms are available in Special Instructions.

Patient financial assistance may be available to those who qualify. Patients who receive a bill from Mayo Clinic Laboratories will receive information on eligibility and how to apply.