

Cardiomyopathy: Deletion/Duplication Panel

Test Code: MD520

Turnaround time: 2 weeks

CPT Codes: 81228 x1, 81479 x1

Condition Description

Dilated Cardiomyopathy

Hereditary dilated cardiomyopathy (DCM) may be inherited in an autosomal dominant, autosomal recessive, or X-linked manner, depending on the gene involved. DCM is characterized by left ventricular enlargement and reduced myocardial contraction force. Typically, DCM presents with one of three features: heart failure, thromboembolic disease, or arrhythmias and/or conduction system disease. Approximately 20-50% of idiopathic dilated cardiomyopathy (those cases not due to acquired causes) are thought to have a genetic cause.

Hypertrophic Cardiomyopathy

Hereditary hypertrophic cardiomyopathy (HCM) is inherited in an autosomal dominant manner. HCM is characterized by left ventricular hypertrophy in the absence of a predisposing cardiac or cardiovascular condition. The manifestation of HCM is extremely variable, even within the same family, and can range from asymptomatic to progressive heart failure. Other features include syncope, presyncope, shortness of breath, chest pain, orthostasis, and palpitations. The onset of HCM is usually during adolescence or young adulthood; however, it can range from infancy to much later in adult life. The prevalence of HCM is approximately 1 in 500 and ~55-70% of cases are caused by a mutation in one of the genes that encode a part of the sarcomere.

Left Ventricular Noncompaction

Familial left ventricular noncompaction (LVNC) is an autosomal dominant or X-linked cardiomyopathy. The distinct diagnostic features of LVNC (a thick, bilayered myocardium, deep intertrabecular recesses, and prominent ventricular trabeculations) are secondary to an arrest of myocardial maturation during embryo development. Individuals with LVNC may be symptomatic or asymptomatic. Major complications of LVNC include heart failure, thromboembolic events, arrhythmias, and sudden cardiac death. Diagnosis can occur prenatally through late adulthood. The manifestation of LVNC is extremely variable, even within the same family. Approximately 30% of isolated LVNC are caused by a mutation in a sarcomere gene.

Restrictive Cardiomyopathy

Restrictive cardiomyopathy (RCM) is a primary myocardial disorder in which the main feature, restrictive ventricular physiology, develops early in the disease. RCM is characterized by inadequate ventricular relaxation during diastole. Onset can range from childhood to late adulthood. Major complications of RCM can include congestive heart failure, cerebrovascular accidents, and arrhythmias. Cardiac restriction may occur secondary to many genetic syndromes, such as Pompe disease and Fabry disease.

Arrhythmogenic Right Ventricular Dysplasia/Cardiomyopathy

Arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVD/C) is an autosomal dominant condition characterized by abnormalities in cardiac structure and rhythm. The fibrofatty replacement of myocardium can predispose affected individuals to ventricular tachycardia and sudden death in young individuals and athletes. Common presenting features include heart palpitation, syncope, and death. Other diagnostic criteria include right ventricular dilation and reduction of right ventricular function, and right ventricular aneurysms. The phenotype of ARVD/C is highly variable and while it primarily affects the right ventricle, it may involve the left ventricle as well.

Catecholaminergic Polymorphic Ventricular Tachycardia

Catecholaminergic polymorphic ventricular tachycardia (CPVT) is characterized by cardiac electrical instability. This instability can be exacerbated by acute activation of the adrenergic nervous system, such as during exercise or extreme emotional events. These episodes have an underlying cause of ventricular tachycardia, which may progress into ventricular fibrillation.

The Cardiomyopathy Panel offered at Emory Genetics Laboratory includes genes that cause each of the above cardiomyopathies, as well as genes that cause genetic syndromes, which have cardiomyopathy as a clinical feature. Syndromic conditions on this panel include Duchenne/Becker muscular dystrophy, Emery-Dreifuss muscular dystrophy, Pompe disease, Fabry disease, Danon disease, Charcot-Marie Tooth, congenital muscular dystrophy, limb girdle muscular dystrophy, Wolff-Parkinson-White syndrome, cardiac glycogenosis, Barth syndrome, familial transthyretin amyloidosis, myofibrillar myopathy, total anomalous venous return, rippling muscle disease, long QT syndrome, skin fragility and woolly hair syndrome, lethal acantholytic epidermolysis bullosa, Naxos disease, and progeria.

References:

- GeneReviews
- Paterick *et al.*, (2012), *J Am Soc Echocardiog*, 25:363-375.
- Peters and Khandheria, (2012), *Curr Cardiol Rep*, 14:381-388.
- Sen-Chowdhry *et al.*, (2010), *Heart Failure Clin*, 6:179-186.

Genes

[ABCC9](#), [ACTC1](#), [ACTN2](#), [ANKRD1](#), [BAG3](#), [BRAF](#), [CASQ2](#), [CAV3](#), [CRYAB](#), [CSRP3](#), [DES](#), [DMD](#), [DSC2](#), [DSG2](#), [DSP](#), [DTNA](#), [EMD](#), [FKTN](#), [GAA](#), [GATAD1](#), [GLA](#), [HRAS](#), [JPH2](#), [JUP](#), [KRAS](#), [LAMA4](#), [LAMP2](#), [LDB3](#), [LMNA](#), [MAP2K1](#), [MAP2K2](#), [MYBPC3](#), [MYH6](#), [MYH7](#), [MYL2](#), [MYL3](#), [MYOZ2](#), [MYPN](#), [NEBL](#), [NEXN](#), [NRAS](#), [PKP2](#), [PLN](#), [PRKAG2](#), [PTPN11](#), [RAF1](#), [RBM20](#), [RIT1](#), [RYR2](#), [SCN5A](#), [SGCD](#), [SOS1](#), [TAZ](#), [TCAP](#), [TMEM43](#), [TNNC1](#), [TNNI3](#), [TNNI2](#), [TPM1](#), [TTN](#), [TTR](#), [VCL](#)

Indications

This test is indicated for:

- Individuals with a cardiomyopathy.

Methodology

Deletion/Duplication Analysis: DNA isolated from peripheral blood is hybridized to a gene-targeted CGH array to detect deletions and duplications. The targeted CGH array has overlapping probes that cover the entire genomic region.

Detection

Deletion/Duplication Analysis: Detection is limited to duplications and deletions. The CGH array will not detect point or intronic mutations. Results of molecular analysis must be interpreted in the context of the patient's clinical and/or biochemical phenotype.

Specimen Requirements

Submit only 1 of the following specimen types

Type: Whole Blood (EDTA)

Specimen Requirements:

EDTA (Purple Top)

Infants and Young Children (2 years of age to 10 years old: 3-5 ml

Older Children & Adults: 5-10 ml

Autopsy: 2-3 ml unclotted cord or cardiac blood

Specimen Collection and Shipping:

Ship sample at room temperature for receipt at EGL within 72 hours of collection. Do not freeze.

Type: DNA, Isolated

Specimen Requirements:

Microtainer

3µg

Isolation using the Perkin Elmer™ Chemagen™ Chemagen™ Automated Extraction method or Qiagen™ Puregene kit for DNA extraction is recommended.

Specimen Collection and Shipping:

Refrigerate until time of shipment in 100 ng/µL in TE buffer. Ship sample at room temperature with overnight delivery.

Related Tests

- Individual gene sequencing analysis is available for *CAV3*, *DES*, *DMD*, *EMD*, *GAA*, *GLA*, *LAMP2*, *LMNA*, *RYR2*, *SGCD*, and *TCAP*.
- Custom diagnostic mutation analysis (KM) is available to family members if mutations are identified by targeted mutation testing or sequencing analysis.
- Prenatal testing is available only for known familial mutations to individuals who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.
- Cardiomyopathy: Sequencing Panel.