

Heart Institute Diagnostic Lab

CAP#: 7518730

CLIA#: 36D2003208

Phone: (513) 803-1751

Fax: (513) 803-1748

Email: HeartDx@cchmc.org

Shipping Instructions

Please enclose a test requisition form with sample. All information must be complete before sample can be processed. Samples may be shipped at room temperature by overnight Federal Express to arrive Monday through Friday.

Ship To:

Cincinnati Children's
Hospital Medical Center
Attn: Heart Institute Diagnostic Lab
240 Albert Sabin Way,
Room S4.381
Cincinnati, OH 45229-3039

LMNA – Associated Dilated Cardiomyopathy

LMNA – Associated Dilated Cardiomyopathy is characterized by left ventricular enlargement, which is often accompanied by heart muscle conduction disease and arrhythmias. It is estimated that mutations in *LMNA* account for 7.5% of familial dilated cardiomyopathy, and 3.6% of idiopathic dilated cardiomyopathy (1). While there are more than 20 genes associated with autosomal dominant dilated cardiomyopathy, *LMNA* mutations are thought to be one of the more common genetic causes. The *LMNA* gene encodes two proteins known as lamin A and lamin C. Both proteins can be found within the nuclear lamina, and are thought to function as structural proteins. It has been hypothesized that mutations in *LMNA* compromise the integrity of the nuclear structure and therefore allow excess apoptosis (2). The *LMNA* gene contains 12 exons and is located on chromosome 1q21.2.

Causative mutations in *LMNA* are estimated to account for 5.9% of all cases of dilated cardiomyopathy(1). *LMNA*-associated dilated cardiomyopathy has an autosomal dominant pattern of inheritance. Penetrance is noted to be age-dependant, with greater than 95% penetrance by the seventh decade of life.

While many genes have been identified to cause autosomal dominant dilated cardiomyopathy, *LMNA* is unique in that it is more commonly seen with conduction system disease. Approximately 95% of individuals with *LMNA*-associated dilated cardiomyopathy are noted to have this additional manifestation (1).

Other diseases associated with *LMNA* include Left ventricular noncompaction, skeletal myopathy, Emery-Dreifuss muscular dystrophy, Limb-Girdle muscular dystrophy, lipodystrophy, and Hutchinson-Gilford progeria syndrome among others.

Indication

LMNA gene testing is utilized to confirm a diagnosis of dilated cardiomyopathy in patients with clinically evident disease. Genetic testing allows for early identification and diagnosis of individuals at greatest risk prior to the expression of typical clinical manifestations.

Methodology:

All 12 exons of the *LMNA* gene, as well as the exon/intron boundaries and portion of untranslated regions of the gene are amplified by PCR. Genomic DNA sequences from both forward and reverse directions are obtained by automatic fluorescent detection using an *ABI PRISM® 3730 DNA Analyzer*. Sequence variants different from National Center for Biotechnology Information GenBank references are further evaluated for genetic significance. If a mutation is identified, a known familial mutation analysis will be available for additional family members.

Sensitivity & Accuracy:

Greater than 98.5% of the mutations in exons 1-12 of *LMNA* are detectable by sequence based methods. Sequencing does not detect deletions or duplications.

References:

1. Parks SB, Kushner JD, Nauman D, Burgess D, Ludwigsen S, Peterson A, et al. Lamin A/C mutation analysis in a cohort of 324 unrelated patients with idiopathic or familial dilated cardiomyopathy. *American Heart Journal*. 2008;156(1):161-9. PMID: 2527054.
2. Capell BC, Collins FS. Human laminopathies: nuclei gone genetically awry. *Nature Reviews Genetics*. 2006;7(12):940-52.

Specimen:

Peripheral blood in EDTA tube

Adult: 5-10mL

Child: 3-5mL

Infant: 1-3mL

For other specimen types, please contact Amy Shikany at 513-803-3317

Turnaround Time:

Full Mutation Analysis 2-4 weeks

Known Mutation Analysis 1-2 weeks

CPT Codes:

Full Gene Sequencing 81406

Additional Family Members 81403