

**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

## **MYL3 – Associated Hypertrophic Cardiomyopathy**

*MYL3* – Associated Hypertrophic Cardiomyopathy (HCM) is characterized by left ventricular hypertrophy in the absence of predisposing cardiac conditions. While there are more than 18 genes associated with autosomal dominant HCM, *MYL3* mutations are thought to comprise 1% of all cases (1). The *MYL3* gene codes for the protein myosin essential light chain (also known as alkali light chain), which plays a role in stabilizing the long alpha-helical neck of the myosin head (2). The *MYL3* gene contains 7 exons and is located on chromosome 3p21.31.

Homozygous mutations in the *MYL3* gene have been associated with restrictive physiology in one consanguineous family with early-onset hypertrophy (3). Approximately 50-65% of individuals with a known or suspected diagnosis of familial HCM have a mutation in one of a number of genes encoding components of the sarcomere and cytoskeleton.

### **Indication**

*MYL3* gene testing is utilized to confirm a diagnosis of HCM 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. If a mutation is identified in an asymptomatic individual, regular and routine outpatient follow up is indicated. If clinically unaffected members of a family with an identified mutation for HCM are found not to carry that mutation, they can be definitely diagnosed as unaffected and reassured that neither they nor their children will be at higher risk compared to the general population to develop symptoms related to HCM. A negative test result in an individual with a known familial mutation also eliminates the need for routine follow up.

## Methodology:

All 6 coding exons of the *MYL3* 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 GeneBank reference 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 1-6 of *MYL3* are detectable by sequence based methods. Sequencing does not detect deletions or duplications.

## References:

1. Pagon RA, Bird TD, Dolan CR, Stephens K, editors. GeneReviews [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2008 Aug 05 [updated 2011 May 17].
2. Poetter, K., Jiang, H., Hassanzadeh, S., Master, S. R., Chang, A., Dalakas, M. C., Rayment, I., Sellers, J. R., Fananapazir, L., Epstein, N. D. Mutations in either the essential or regulatory light chains of myosin are associated with a rare myopathy in human heart and skeletal muscle. *Nature Genet.* 13: 63-69, 1996.
3. Olson, T. M., Karst, M. L., Whitby, F. G., Driscoll, D. J. Myosin light chain mutation causes autosomal recessive cardiomyopathy with mid-cavitary hypertrophy and restrictive physiology. *Circulation* 105: 2337-2340, 2002.

## 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 81405

Additional Family Members 81403