

Hypertrophic Cardiomyopathy via Sequential Testing of Eight Sarcomeric Genes

Panel 1 Only-Test #191 Panel 2 Only-Test #192 Panel 3 only-Test #193 All Three Panels-Test #190

Brief Description of Clinical Features: Hypertrophic cardiomyopathy (HCM, OMIM # 192600) is a primary disease of the cardiac muscle characterized by idiopathic hypertrophy of the left ventricle, although hypertrophy of the right ventricle may occur occasionally (Fifer and Vlahakes *Circulation* 117:429-439, 2008). HCM is distinguished by an extensive clinical variability between individuals. Symptoms include dyspnea, exercise intolerance, chest pain, palpitations, arrhythmia, atrial fibrillation, syncope and sudden death (Maron et al *N Engl J Med* 316:780-789, 1987). Additional features include left ventricular outflow tract obstruction, which is associated with increased risk for heart failure (Ommen et al. *J Am Coll Cardiol* 46:470-476, 2005). HCM affects 1/500 people worldwide. See also the Hypertrophic Cardiomyopathy Association (<http://www.4hcm.org/>) and Cirino and Ho (*GeneReviews*, 2009, www.genetests.org).

Genetics: HCM is inherited in an autosomal dominant manner. It is caused by mutations in various genes that encode sarcomeric proteins. Over 500 different pathogenic mutations, mostly missense, were detected in 8 genes, accounting for 74-94% of all HCM cases with known genetic cause (~60% of total HCM cases) (Hershberger et al. *Circ Heart Fail* 2:253-261, 2009). Mutations were identified in both familial and sporadic cases, with similar distribution (Richard et al. *Circulation* 107:2227-2232, 2003). In addition to these 8 genes, PreventionGenetics also offers tests for genes that are very rarely mutated in HCM patients. These include the *TTN*, *MYH6*, *TCAP*, *VCL*, *ACTN2*, *PLN*, *CSRP3*, *TNNC1* and *CAV3* genes.

Description of These Tests: PreventionGenetics offers sequencing of each of the 8 genes individually, or the Panels described here. These tests involve bidirectional DNA sequencing of all coding exons of the genes as well as ~50 bp of flanking-coding DNA on either side. **Reference Sequences:**

Gene	<i>MYBPC3</i>	<i>MYH7</i>	<i>TNNT2</i>	<i>TNNI3</i>	<i>TPM1</i>	<i>MYL2</i>	<i>MYL3</i>	<i>ACTC1</i>
Genomic NC_	000011.9	000014.8	000001.10	000019.9	000015.9	000012.11	000003.11	000015.9
mRNA NM_	000256.3	000257.2	001001430	000363.4	001018020.1	000432.3	000258.2	005159.4
Protein NP_	000247.2	000248.2	001001430.1	000354.4	001018020.1	000423.2	000249.1	005150.1

Panel 1 Only: Sequential sequencing of all coding exons of *MYBPC3* and *MYH7* genes; detects ~80% of known mutations.

Panel 2 Only: Sequencing of all coding exons of *TNNT2*, *TNNI3* and *TPM1* genes; detects ~12% of known mutations.

Panel 3 Only: Sequencing of all coding exons of *MYL2*, *MYL3* and *ACTC1* genes; detects ~5% of known mutations.

Indications for Test: Patients with symptoms suggestive of HCM (OMIM 192600).

Sensitivity of Test: Together, these eight tests may detect mutations in up to 60% of all HCM patients (~90% of patients with detectable mutations) (Hershberger et al. *Circ Heart Fail* 2:253-261, 2009).

Turn Around Time: Maximum of 40 days, although many tests are completed in 2-3 weeks.

Specimen Requirements: See bottom of page 2 of Requisition Form

Prices and CPT Codes:

CPT	Description	Panel 1 Only	Panel 2 Only	Panel 3 Only	Panels 1, 2 and 3
83890	Sample Ascertainment	\$ 30 (x1)	\$ 30 (x1)	\$ 30 (x1)	\$ 30 (x1)
83891	DNA Isolation	\$ 40 (x1)	\$ 40 (x1)	\$ 40 (x1)	\$ 40 (x1)
83898	Amplification	\$ 930 (x67)	\$ 590 (x31)	\$ 410 (x20)	\$2060 (x118)
83904	Sequencing	\$1390 (x67)	\$ 880 (x31)	\$ 620 (x20)	\$3090 (x118)
83894	Separation	\$ 110 (x1)	\$ 80 (x1)	\$ 60 (x1)	\$ 200 (x1)
83912	Interpretation/Report	\$ 130 (x1)	\$ 90 (x1)	\$ 80 (x1)	\$ 160 (x1)
	Totals	\$2630	\$1710	\$1240	\$5580

Accreditation Info. CLIA ID #: 52D1027685 (expires 1/18/11) (CAP#: 7185561, AU ID: 1407125 expires 12/20/10)

Contact for info: Dr. Khemissa Bejaoui, khemissa@preventiongenetics.com, www.preventiongenetics.com