

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 70 days.

Specimen Requirements: See page 4 of the 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 1/18/13) (CAP#: 7185561, AU ID: 1407125 expires 12/20/12)

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