

## Hypertrophic Cardiomyopathy via *CSRP3* Gene Sequencing -- Test #196

**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 with regards to the age of onset, pattern and extent of hypertrophy, and prognosis. 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 and cardiovascular death (Ommen et al. *J Am Coll Cardiol* 46:470-476, 2005). HCM affects 1 in 500 people worldwide (Maron et al, *Circulation*, 92, 785-789, 1995). See also the Hypertrophic Cardiomyopathy Association (<http://www.4hcm.org/>) and Cirino and Ho, (*GeneReviews*, 2009, [www.genetests.org](http://www.genetests.org)).

**Genetics:** HCM is a heterogeneous genetic disease that is inherited in an autosomal dominant manner. It is caused by mutations in various genes, most of which encode sarcomeric proteins. Defects in twelve genes, including the *CSRP3* gene (Geier and Perrot *Circulation* 107:1390-1395, 2003; Bos et al. *Mol Genet Metab* 88:78-85, 2006), account for approximately 60% of all HCM cases. Mutations were identified in both familial and sporadic cases, with similar distribution. Mutations identified in sporadic cases were either nonpenetrant or occurred *de novo* (Richard et al. *Circulation* 107:2227-2232, 2003). Some patients with severe phenotype were shown to have more than one mutation, either in two different genes or in the same gene (Richard et al. 2003). To date 9 different *CSRP3* causative mutations were reported in patients with HCM. These include 7 missense mutations, one small deletion and one indel. In addition to HCM, heterozygous *CSRP3* mutations were found in patients with dilated cardiomyopathy (DCM) (Knöll et al. *Cell* 111:943-955, 2002).

**Description of This Particular Test:** The *CSRP3* gene encodes the muscle LIM protein (MLP), a cardiac Z disc protein. This test involves bidirectional DNA sequencing of all 5 coding exons and splice sites of the *CSRP3* gene. The full coding sequence of each exon plus ~ 50 bp of flanking DNA on either side are sequenced.

**Reference Sequences:** Genomic: NC\_000011.9 mRNA: NM\_003476.3 Protein: NP\_003467.1(CCDS 7848.1)

**Indications for Test:** Patients with HCM (OMIM 192600) and no mutations in the genes that are frequently mutated in HCM patients (See Test # 190), and patients with DCM (OMIM 612124).

**Sensitivity of Test:** This test allows the detection of mutations in rare cases of patients with HCM (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 page 4 of the Requisition Form.

**Price: Sequencing of *CSRP3* Gene, Exons 2 - 6 \$ 470**

**CPT Codes:**

Sample Ascertainment x1	83890 \$ 30	DNA Isolation x1	83891 \$ 40
Amplification x 5	83898 \$ 120	Sequencing x 5	83904 \$ 170
Separation x1	83894 \$ 40	Interpretation/Report x1	83912 \$ 70

**Accreditation Info. CLIA ID #: 52D1027685** (expires 1/18/13) (CAP#: 7185561, AU ID: 1407125 expires 12/20/12)

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