Facts on Hypertrophic Cardiomyopathy (HCM)

- HCM is a dominantly inherited disease affecting 1 in 500 individuals.

- HCM is caused by mutations in any one of at least 12 genes.
  - Mutations in TNNT2, TNNI3, TPM1, MYBPC3, MYH7, MYL2, MYL3, or ACTC account for about 60% of familial HCM.
  - Mutations in PRKAG2 or LAMP2 account for about 1% of all familial HCM and for about 50% of HCM with ventricular pre-excitation.

- HCM leads to death from severe complications in about 10% of patients.
  - Of 744 HCM patients, 6% died from SCD (mean age 45), 4% from congestive heart failure (mean age 56), and 2% from stroke (mean age 73).

- HCM is the most common cause of sudden cardiac death (SCD) in young adults, including trained athletes. Affected individuals are often unaware of their condition.
  - About a third of SCD in athletes is due to HCM (134 individuals, mean age 17).

- Extensive cardiac screening at regular intervals can identify patients at high risk for SCD, who may benefit from implantation of a cardioverter-defibrillator.
  - ICDs corrected potentially lethal arrhythmias in 20% of 506 high-risk HCM patients.

- Children who are genetically predisposed to HCM may be advised not to participate in certain competitive sports.

- Genetic testing can confirm a diagnosis of HCM in the index patient for a family and identify family members with a predisposition for HCM at any age.

- Genetic testing can distinguish metabolic HCM from sarcomeric HCM, informing prognosis and genetic counseling of HCM patients.

- Genetic testing is the only reliable way to identify unaffected family members, who do not need regular cardiac screening for risk factors of SCD.
  - Physical examination alone cannot rule out HCM since symptoms can develop at any time during life.
Using Genetic Testing to Diagnose Hypertrophic Cardiomyopathy

**Indications:**
- Clinical diagnosis of hypertrophic cardiomyopathy (HCM)
- Unexplained cardiovascular symptoms such as chest pain, dyspnea and/or history of syncopal episodes in young adults, especially athletes
- Family history of sudden cardiac death (SCD) in individuals under age 45

**Benefits:**
Genetic testing for HCM can:
- confirm a clinical diagnosis of HCM.
- distinguish between different forms of HCM
- identify at-risk family members who should undergo regular cardiac screening
- identify family members who do not need to undergo regular cardiac screening

**Background:**
- Hypertrophic cardiomyopathy (HCM), which is characterized by a thickening of the heart muscle, occurs at a prevalence of 1 in 500 (0.2%) and typically shows dominant mode of inheritance.¹,²
- HCM has a benign prognosis in most patients, but leads to severe complications including heart failure, stroke, and cardiac arrest in about 10% of patients.¹,²
- HCM the most common cause of SCD in young adults, including competitive athletes.³
- Extensive cardiac screening at regular intervals can identify patients at high risk for SCD, who may benefit from implantation of a cardioverter-defibrillator.⁴
- About 60% of all familial HCM is associated with mutations in any one of at least 10 different components of the sarcomer.⁵,⁶
- About 1% of HCM and up to 50% of HCM with ventricular pre-excitation is due to cytoplasmic or lysosomal glycogen accumulation in cardiac myocytes (metabolic HCM).⁷,⁸
- Metabolic HCM may differ from sarcomeric HCM with regard to prognosis and mode of inheritance.⁷,⁸

**References:**

**Ordering Information:** Please see other side.
Ordering Information for Hypertrophic Cardiomyopathy Testing

Guidelines for Test Selection

Ordering Information for Single Gene Tests

<table>
<thead>
<tr>
<th>Gene(s)</th>
<th>CPT Codes</th>
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Ordering Information for Multi-Gene Panels*

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Reflexive testing option:
TNNT2, MYH7, MYBPC3 → TPM1, TNNI3, MYL2, MYL3, ACTC (reflexing occurs if no (probable) disease variant is found) 190350

*For multi-gene panels, a summary report will be issued in addition to an abbreviated report for each individual gene.

Family Testing (single amplicon)
(applies to all genes) 83891(1) 83892(1) 83898(1) 83904(2) 83909(2) 83912(1) use single-gene test code

Test Methodology and Sample Requirements

- Amplification by polymerase chain reaction (PCR); sequencing of entire protein-coding region
- For blood samples: 2mL whole blood in EDTA tube (lavender top)
- Samples can be stored briefly at 4°C, but should be shipped on day of collection.
- For buccal swab samples: (only accepted for family testing) Please contact client services at 1-866-647-0735 for instructions.
- All sample types should be shipped overnight at room temperature.
- To request a sample shipping kit, please call 1-866-647-0735.

Turn-around Times

Turn-around times typically range from 7 to 21 days of receipt of sample and all required forms, but may vary depending on test volume and test-specific technical difficulties. Current TATs are posted on our website. Please schedule patient follow-up appointments for discussion of test results conservatively at 6 weeks.

For more information, please contact Correlagen Diagnostics, Inc., at 1-866-647-0735 or visit us on the web at www.correlagen.com.
Hypertrophic Cardiomyopathy – an Overview

Introduction

Hypertrophic cardiomyopathy (HCM), which occurs at a prevalence of 1 in 500 (0.2%), is characterized by a thickening of the heart muscle that can lead to severe cardiac problems such as progressive heart failure, embolic stroke, and sudden cardiac death (SCD) (1-4). Notably, HCM is the most common cause of SCD in young adults, who are often unaware of their underlying condition. Early diagnosis of HCM is important, since at-risk individuals may be advised not to participate in competitive sports and should undergo regular cardiac screening to assess the risk of SCD (5). In high-risk patients, use of an implantable cardioverter-defibrillator (ICD) may help to prevent SCD (6). Since most cases of HCM are familial, regular screening of family members of known patients can help to identify individuals at increased risk for HCM early in life (5,7). However, cardiac screening cannot reliably identify unaffected family members, because clinical diagnosis is based on the appearance of HCM-related symptoms, which may occur at any age. Since HCM has been associated with dominant mutations in any one of at least 12 genes, genetic testing can facilitate the diagnosis of HCM and allow for accurate identification of both affected and unaffected family members (8,9). Extensive cardiac screening at regular intervals can then be limited to affected family members. In addition, genetic testing can confirm presence of the metabolic subtype of HCM, which may differ in both prognosis and mode of inheritance from the more common sarcomere-related HCM (10).

Molecular Pathophysiology

Most HCM is caused by defects in the cardiac sarcomere – the contractile unit of the heart muscle (11). The sarcomere is built from thick and thin filaments, which are arranged in an overlapping fashion. Thick filaments are composed primarily of myosin, along with associated myosin binding proteins C, H, and X. Thin filaments are composed of cardiac actin, α-tropomyosin, and troponins C, I, and T. A giant protein, titin, provides a scaffold for the thick and thin filaments. When thick filaments slide along thin filaments, the muscle shortens. This contractile motion is driven by interaction of the myosin motor protein with actin and triggered by transient increases in intracellular Ca\(^{2+}\) concentration. The response to Ca\(^{2+}\) is regulated by the cardiac troponin-tropomyosin complex in sarcomeric thin filaments. The myosin light chain kinase and myosin-binding protein-C also play a role in the modulation of cardiac contractility.

HCM has been linked to mutations in almost every protein within the sarcomere, including thick filament proteins MYH7, MYL2, MYL3, and MYBPC3 and thin filament proteins ACTC, TNNT2, TNNI3, and TPM1. Mutations in the genes coding for these eight proteins are estimated to account for about 60% of all familial cases of HCM (Table 1).

<table>
<thead>
<tr>
<th>Gene (Protein)</th>
<th>% HCM</th>
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<tr>
<td><strong>Sarcomere-related HCM</strong></td>
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<tr>
<td>TNNT2 (cardiac troponin T)</td>
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<td>TNNI3 (cardiac troponin I)</td>
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<tr>
<td>TPM1 (α-tropomyosin)</td>
<td>&lt;5</td>
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<tr>
<td>MYBPC3 (myosin binding protein C)</td>
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<tr>
<td>MYH7 (cardiac myosin heavy chain, beta)</td>
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<tr>
<td>MYL3 (cardiac myosin light chain, essential)</td>
<td>&lt;1</td>
</tr>
<tr>
<td>ACTC (α-cardiac actin)</td>
<td>&lt;1</td>
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<tr>
<td><strong>Metabolic HCM</strong></td>
<td></td>
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<tr>
<td>PRKAG2 (AMP-activated protein kinase)</td>
<td>&lt;1</td>
</tr>
<tr>
<td>LAMP2 (lysosome–associated membrane protein)</td>
<td>&lt;1</td>
</tr>
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</table>

A less common type of HCM, known as metabolic HCM, is not related to defects in the cardiac sarcomere, but due to glycogen accumulation in cardiac myocytes (10). Metabolic HCM is typically associated with ventricular pre-excitation and atrial fibrillation (Wolff-
Parkinson-White syndrome, WPW), presumably because glycogen-filled myocytes can serve as accessory conduction pathways between the atria and the ventricles. Over time, glycogen accumulation may lead to cell death and progressive conduction defects. Mutations in the gamma-2 regulatory subunit of AMP-activated protein kinase 2 or in lysosome-associated membrane protein 2 are believed to account for about 1% of all HCM and for up to 50% of HCM with ventricular pre-excitation (Table 1).

**Clinical Presentation**

The initial clinical presentation of patients with HCM is widely variable and includes cardiac arrhythmias, exercise-induced hypotension, systolic heart murmur with bifid arterial pulse, pulmonary congestion and/or fatigue, a history of syncope or near syncope, cardiac arrest, or even SCD (1). In young athletes, the two most common complaints are chest pain and exertional dyspnea (4). Adolescent patients are at higher risk of SCD, while older patients are more likely to develop progressive heart failure or embolic stroke (3). Initial presentation typically occurs during adolescence, but symptoms may also appear during childhood or be delayed to adulthood (5). Most patients exhibit left-ventricular hypertrophy (LVH), and 75-95% of patients show an abnormal EKG pattern. Between 20-25% of affected individuals also suffer from chronic atrial fibrillation, which is associated with an increased risk of embolic stroke. Ventricular arrhythmias, which can lead to SCD, also may occur. Some HCM patients suffer progressive heart failure, and 5-10% of patients experience LV wall thinning and systolic dysfunction that resembles dilated cardiomyopathy. Over time, HCM causes scarring, fibrosis, and cellular disarray in the myocardium and narrowing of the coronary arteries (4).

Metabolic HCM is typically associated with ventricular pre-excitation and frequently presents with WPW (10). Chronic atrial fibrillation leads to an increased risk of embolic stroke, and progression to conduction defects requiring pacemaker implantation is common (12). HCM due to mutations in LAMP2 – also known as Danon disease – presents differently in males and females, probably due to its unusual X-linked dominant mode of inheritance (13). In males, clinical symptoms typically first appear in childhood or adolescence and, in addition to cardiac manifestations such as HCM, WPW, and atrioventricular block, include skeletal myopathy, ophthalmic abnormalities, mild mental retardation, and hepatic involvement (14). Females typically first present in their thirties or forties, with either hypertrophic or dilated cardiomyopathy and few extra-cardiac manifestations. Prognosis is poor in both males and females, with rapid progression to heart failure.

**Diagnosis**

Diagnosis of HCM is most commonly based on an observation of left ventricular hypertrophy (LVH), often disproportionately affecting the ventricular septum, that cannot be explained by another disease such as aortic stenosis (1). LVH associated with outflow obstruction is indicated by a heart murmur and/or bifid arterial pulse, while LVH without outflow obstruction is most reliably diagnosed by 2-dimensional echocardiography or MRI. LVH can range from mild (~13-15 mm) to severe (30-60 mm) and may increase or decrease significantly throughout life. “Athlete’s heart,” a mild, benign thickening of the heart muscle often observed in trained athletes, can complicate the diagnosis of HCM because it resembles mild LVH caused by HCM. Diagnosis of WPW is based on the characteristic EKG pattern caused by ventricular pre-excitation – a shortened PR interval and/or a widened QRS complex with a delta wave (10). Presence of skeletal myopathy and elevated creatine kinase levels in males may be indicative of Danon disease (10,13). Since published studies have established a causal relationship between HCM and certain variants of the genes TNNT2, TNNI3, TPM1, MYBPC3, MYH7, MYL2, MYL3, ACTC, PRKAG2, and LAMP2, genetic testing not only can confirm a diagnosis of HCM in an affected index patient, but also distinguish family members who are affected but presymptomatic from those who are not affected. In addition, genetic testing can identify cases of metabolic HCM and clarify the mode of inheritance, with important implications for prognosis and genetic counseling.
Once patients have been diagnosed with HCM, they should undergo periodic risk assessment for SCD to guarantee timely recognition of risk factors (2,4,5,7). The two strongest risk factors are prior cardiac arrest and spontaneous sustained ventricular tachycardia; patients who have experienced either are at high risk of SCD (1). Additional risk factors include severe LVH (>30 mm), LVH outflow tract obstruction of >30mm Hg, abnormal blood pressure response during exercise, non-sustained ventricular tachycardia, and history of syncope along with a family history of SCD. HCM patients with two or more of these risk factors are also considered high risk; those with just one are moderate risk; and those with none are low risk (15).

**Treatment**

Treatment depends on symptoms and/or risk of SCD. Chronic atrial fibrillation is treated with anticoagulant therapy to prevent clotting and embolic stroke and with electrical or pharmaceutical cardioversion to control arrhythmias. Ventricular pre-excitation can be controlled by medication and may be cured by surgical or radiofrequency catheter ablation of the accessory pathway. Severe outflow obstruction is treated surgically by ventricular septal myotomy-myectomy or non-surgically by alcohol septal ablation or chronic dual chamber pacing. Atrioventricular block can be effectively controlled by pacemaker implantation. Progressive heart failure is treated pharmacologically with verapamil or β-blockers or, at its end stage, surgically by heart transplantation, which presents the only effective treatment for LAMP2-related cardiomyopathy (13). For patients at high risk for SCD, an ICD may be advised (6).

Of note, autosomal dominant mutations in MYH7, MYBPC3, TNNT2, TPM1, and ACTC are also associated with familial dilated cardiomyopathy; autosomal dominant mutations in TNNI3 have been linked to familial restrictive cardiomyopathy; and at least one autosomal recessive mutation in TNNI3 has been associated with familial dilated cardiomyopathy (11,16). PRKAG2-related cardiac disease is phenotypically variable and can range from late-life onset of conduction defects to fatal congenital cardiac glycogenosis (17,18).

**References**


Requisition Form

Please send sample and completed forms to →
(Ship sample overnight at room temperature.)

Is this a family test for a known familial mutation? □ yes □ no

Familial mutation □ Gene (eg, MYH7) □ Variant (eg, c.746G>A) □ Exon (eg, x9)

Was the index patient* tested at Correlagen? □ yes □ no

(*Family member in whom familial mutation was identified.) If yes: Please complete Index Patient Section on right.

Relationship of current patient to index patient

Patient Information (current patient)

Name □ First Name MI Last Name
Date of Birth / / month day year Sex □ male □ female
Social Security #
Address □ Number □ Street □ Apt.
Address □ City □ State □ Zip
Phone day ( ) evening ( )

Physician’s Identifier for Patient

Physician Information

Medical Specialty

Name □ First Name □ Last Name
Institution Name
Address □ Number □ Street □ Building/Suite
Address □ City □ State □ Zip
Phone ( ) Fax ( )
e-mail

Cancellation Policy:

Cancellation requests must be submitted in writing by the ordering physician. Cancellation requests will only be accepted if received before specimen testing begins.

For more information, please call: 1-866-647-0735

Sample Specifications

Date and Time of Sample Collection (required):

Sample Type (check one):

□ Blood samples:
  ○ 2 mL whole blood in EDTA (lavender-top tube)
  ○ Can be stored briefly at 4°C, but should be shipped on day of collection

□ Buccal swabs:
  ○ Please contact client services at 1-866-647-0735 for instructions.

□ DNA samples:
  Preferably ≥ 1 µg at 50 ng/µl in TE
  Actual total amount of DNA: µg
  Actual DNA concentration: ng/µl

Accession Number (Internal use)
Dear client,

Please take a moment to fill out this survey. Your responses will help us to serve you even better in the future.

Thank you from your Correlagen team.

How did you hear about us?

☐ Through a colleague  
☐ Through a patient  
☐ Through a patient advocacy group  
☐ Through the news media  
☐ Through the internet  
  ☐ Search engine (such as Google, Yahoo, etc)  
  ☐ Google Ad  
  ☐ Other:__________________________
☐ Through an e-mail from us  
☐ Through a phone call from us  
☐ Other:__________________________

Have you ordered from us before?

☐ Yes

  How would you rank our services?

  Please circle one number (1=unsatisfactory; 5=excellent)

  Client services
  1  2  3  4  5
  Billing
  1  2  3  4  5
  Turn-around times
  1  2  3  4  5
  Result reports
  1  2  3  4  5
  Informational material
  1  2  3  4  5

☐ No

Which other genetic tests would you like us to offer?

____________________________________________________________________________________
____________________________________________________________________________________

Other comments:

____________________________________________________________________________________
____________________________________________________________________________________

Would you like someone to call you to discuss your responses?

☐ Yes
☐ No
Atrial Septal Defect with Atroventricular Block
- # 190401  NKX2-5

Dilated Cardiomyopathy
- # 190599  TNNT2, MYBPC3, MYH7, TPM1, ACTC
- # 190501  TNNT2
- # 190502  TNNI3
- # 190503  TPM1
- # 190504  MYBPC3
- # 190505  MYH7
- # 190506  ACTC

Early-Onset Coronary Heart Disease
- # 190199  LDLR, APOB
- # 190101  LDLR
- # 190102  APOB

Hypertrophic Cardiomyopathy
- # 190398  TNNT2, MYBPC3, MYH7
- # 190397  TPM1, TNNI3, MYL2, MYL3, ACTC
- # 190396  TNNT2, MYBPC3, MYH7, TPM1, TNNI3, MYL2, MYL3, ACTC
- # 190395  PRKAG2, LAMP2
- # 190350  Reflexive-testing option: TNNT2, MYBPC3, MYH7
  If no (probable) disease variant found: TPM1, TNNI3, MYL2, MYL3, ACTC
  - # 190301  TNNT2
  - # 190302  TNNI3
  - # 190303  TPM1
  - # 190304  MYBPC3
  - # 190305  MYH7
  - # 190306  MYL2
  - # 190307  MYL3
  - # 190308  ACTC
  - # 190309  PRKAG2
  - # 190310  LAMP2

Arrhythmogenic Right Ventricular Dysplasia
- #190799  PKP2, DSP, DSC2, DSG2
- #190701  PKP2
- #190702  DSP
- #190703  DSC2
- #190704  DSG2

Marfan Syndrome
- #190601  FBN1

Pulmonic Stenosis
- # 190201  PTPN11

Use same test code for full gene test or single variant test.
# Payment Form

## Institutional Billing

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## Commercial Insurance

Correlagen has established the Capped Patient-Payment Plan (CPPP) to assist patients covered by most commercial insurance. The CPPP limits the financial responsibility of the patient to 15% of the total cost plus any portion of the test cost that is applied by the insurance company to the patient's annual deductible. To participate in the CPPP, patients must be pre-qualified prior to testing (contact a Client Services Representative to get pre-qualified). Once pre-qualified, patients need to complete the information below and provide the 15% payment before testing is initiated. Patients choosing not to participate in the CPPP will be responsible for all charges not covered by their insurance carrier within 60 days of claim submission.

Note: a higher CPPP rate applies for family testing. See http://www.correlagen.com/resources/billing.jsp for CPPP details and exceptions.

### Commercial Insurance (required)

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<td>Phone</td>
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<tr>
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</tbody>
</table>

**Please include a copy of both sides of the insurance card (required).**

## Payment by Check/Credit Card (Credit card charges may be applied for self-pay, CPPP co-pays and any applicable deductibles)

- **Check or money order enclosed** $ ____________
- **Credit Card**
  - Master Card [ ]
  - Visa [ ]
  - Card Number ________
  - Expiration DateMonth ________ Year ________
  - Billing Address Number ________ Street ________ City ________ State ________ Zip ________
  - Please bill my credit card for the amount of $ ____________

**Signature (required) Date**
To
Name of Insurance Company: _______________________________________________________

Request for coverage of diagnostic DNA-sequence analysis of the genes

☐ TNNT2  ☐ TNNI3  ☐ TPM1  ☐ MYBPC3  ☐ MYH7  ☐ MYL2  ☐ MYL3  ☐ ACTC
☐ PRKAG2  ☐ LAMP2

For the purpose of
☐ confirming a diagnosis of hypertrophic cardiomyopathy
☐ evaluating presence or absence of a familial mutation known or believed to be associated with hypertrophic cardiomyopathy.

Indicated by
☐ presence or history of clinical symptoms of hypertrophic cardiomyopathy:

______________________________________________________________________________

☐ family history (indicative) of hypertrophic cardiomyopathy

Regarding my patient
Name of patient: ________________________________________________________________

Insurance number of patient: ________________________________________________________

Name of primary insurance holder: __________________________________________________

Group Policy Number: _____________________________________________________________

Hypertrophic cardiomyopathy (HCM), which occurs at a prevalence of 1 in 500, is characterized by a thickening of the heart muscle leading to decreased cardiac function. About 20% of patients suffer debilitating cardiac symptoms, and about 10% die from congestive heart failure, embolic stroke, or sudden cardiac death (SCD). Since HCM has been associated with mutations in any one of a number of genes, genetic testing can confirm a clinical diagnosis of HCM. Genetic testing can also inform prognosis and genetic counseling, which may vary with the underlying genetic cause. In addition, genetic testing can facilitate family testing for this dominantly inherited disease. Once the familial mutation has been identified in the index patient for a family, genetic testing can identify family members affected with or predisposed to HCM (mutation carriers) and family members who are not at increased risk for HCM (non-mutation carriers). Of note, genetic testing is the only way to differentiate presymptomatic affected family members, who must regularly undergo extensive cardiac screening, from unaffected family members, who do not require further screening. Based on the results of genetic testing, regular extensive cardiac screening for risk factors of sudden cardiac death can be limited to affected family members.

I am choosing Correlagen Diagnostics as the provider of genetic testing services, since this CLIA-certified testing laboratory offers reliable sequencing services, consistent variant analysis, and detailed result reporting with short turn-around times. Since known HCM-associated mutations are spread throughout the genes linked to HCM, Correlagen sequences the entire coding region of each specified gene in the index patient. Coding regions are amplified and sequenced in segments (amplicons). If the familial HCM-associated mutation is known, only the amplicon harboring the familial mutation is amplified and sequenced. At least 60% and up to 80% of all HCM cases are estimated to be due to mutations in the genes TNNT2 (5-20%), TNNI3 (<5%), TPM1 (<5%), MYBPC3 (20-40%), MYH7 (30-50%), MYL2 (<3%), MYL3 (<1%), ACTC (<1%), and PRKAG2 and LAMP2 (1% of HCM, <50% of HCM with ventricular pre-excitation).

In summary, I believe that genetic testing for HCM will allow me to provide better care for my patient and will prove to be a cost-effective measure. Please let me know if you have any further questions.

Sincerely,

________________________  ___________________________           _______________       _____
  Signature    Name (printed)    Tel. No. Date
## Clinical Information Form for Cardiomyopathies (HCM, DCM, ARVD/C)

### Patient:

**First Name** | **M** | **Last Name**
--- | --- | ---

### Medical History:

<table>
<thead>
<tr>
<th>Item</th>
<th>yes</th>
<th>No</th>
<th>Age at onset</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>h/o Cardiac arrest</td>
<td>☐</td>
<td>☐</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chest pain / dyspnea / syncpoe</td>
<td>☐</td>
<td>☐</td>
<td></td>
<td>please specify</td>
</tr>
<tr>
<td>h/o Heart murmur</td>
<td>☐</td>
<td>☐</td>
<td></td>
<td></td>
</tr>
<tr>
<td>h/o Cardiac arrhythmias</td>
<td>☐</td>
<td>☐</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exercise intolerance</td>
<td>☐</td>
<td>☐</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diagnosis of cardiomyopathy</td>
<td>☐</td>
<td>☐</td>
<td></td>
<td>please specify type of cardiomyopathy</td>
</tr>
<tr>
<td>Other (please specify)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Physical Examination Data:

<table>
<thead>
<tr>
<th>Item</th>
<th>Date</th>
<th>Value (circle units)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height</td>
<td>MM/DD/YY</td>
<td>cm/inches</td>
<td></td>
</tr>
<tr>
<td>Weight</td>
<td>MM/DD/YY</td>
<td>kg/pounds</td>
<td></td>
</tr>
<tr>
<td>Blood pressure</td>
<td>MM/DD/YY</td>
<td>Systolic: mm Hg</td>
<td>Diastolic: mm Hg</td>
</tr>
<tr>
<td>Heart murmur</td>
<td>MM/DD/YY</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skeletal myopathy</td>
<td>MM/DD/YY</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Laboratory Test Results:

<table>
<thead>
<tr>
<th>Item</th>
<th>Date</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>EKG</td>
<td>MM/DD/YY</td>
<td></td>
</tr>
<tr>
<td>-- ? Ventricular pre-excitation</td>
<td>MM/DD/YY</td>
<td></td>
</tr>
<tr>
<td>-- ? Epsilon waves</td>
<td>MM/DD/YY</td>
<td></td>
</tr>
<tr>
<td>Echocardiogram/MRI</td>
<td>MM/DD/YY</td>
<td></td>
</tr>
<tr>
<td>-- ? Right ventricular dilation</td>
<td>MM/DD/YY</td>
<td></td>
</tr>
<tr>
<td>Ambulatory EKG (Holter) monitoring</td>
<td>MM/DD/YY</td>
<td></td>
</tr>
<tr>
<td>Blood pressure response during exercise</td>
<td>MM/DD/YY</td>
<td></td>
</tr>
<tr>
<td>Creatine kinase [U/L]</td>
<td>MM/DD/YY</td>
<td></td>
</tr>
<tr>
<td>Other (please specify)</td>
<td>MM/DD/YY</td>
<td></td>
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</tbody>
</table>

### Current Therapy:

<table>
<thead>
<tr>
<th>Item</th>
<th>Start Date</th>
<th>Comments (Dosing, if applicable)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Implantable cardioverter-defibrillator</td>
<td>MM/DD/YY</td>
<td></td>
</tr>
<tr>
<td>Pacemaker</td>
<td>MM/DD/YY</td>
<td></td>
</tr>
<tr>
<td>Other (please specify)</td>
<td>MM/DD/YY</td>
<td></td>
</tr>
</tbody>
</table>

### Family History:

<table>
<thead>
<tr>
<th>Relationship</th>
<th>Cardio-mopathy</th>
<th>Age at onset</th>
<th>Cardiac Arrhythmias</th>
<th>Age at onset</th>
<th>Sudden Cardiac Death</th>
<th>Age at occurrence</th>
<th>Other Cardiac Symptoms (please specify)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>☐</td>
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</tr>
</tbody>
</table>

### Comments:

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Cardiomyopathies ClinInfo 11/08
Informed Consent for Genetic Testing

I hereby request genetic testing by DNA analysis for the following condition:

I understand that the purpose of the DNA test is to look for the presence of abnormalities (often called "variants" or "mutations") in one or more genes that may be associated with the condition specified above.

I understand that a sample of blood will be obtained from me and/or individuals for whom I am authorized to make medical decisions by removing blood from a vein, a procedure that carries very little risk. I give permission to collect blood samples from the individuals named below, to be used for DNA testing for the condition specified above:

<table>
<thead>
<tr>
<th>Child’s Name</th>
<th>Date of Birth</th>
<th>Sex</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

I understand and agree that:

1. By signing this consent, I authorize my doctor to forward my blood, DNA, or tissue sample as well as relevant clinical information about me and about members of my family to Correlagen Diagnostics, Inc. I understand that the testing laboratory needs this clinical information to provide the most accurate interpretation of my test results.

2. While genetic testing is a valuable tool, it does not always give a definite answer. In some cases, the DNA test may not detect an abnormality, although an abnormality may still be present. This event may be due to an inability of the current technology to identify certain types of abnormalities in the gene(s). In other cases, the significance of an abnormality detected by the DNA test for the condition specified above may be uncertain. Thus, the DNA test is not 100% accurate, and the significance of the results will be reported as a probability of association with the condition specified above. Consulting a doctor or genetic counselor is recommended to learn the full meaning of the results.

3. DNA testing performed on a child and a child’s parents might discover non-paternity (a situation where the acknowledged father is not the biological father) or some other previously unknown information about family relationships, such as adoption.

4. The results of this test will be released only to the physician ordering the test or to persons designated by me, in writing, unless otherwise required by law.
5a. Correlagen Diagnostics, Inc, may contact me if it subsequently learns new information that affects the interpretation of previously reported test results. Correlagen Diagnostics, Inc, will make reasonable efforts to contact me through the physician that ordered the test, unless I designate in writing another person authorized to be contacted.

5b. I indicate my desire to opt out of being contacted if Correlagen Diagnostics, Inc, subsequently learns new information that affects the interpretation of previously reported test results, by checking this box: ☐

6a. The sample will be retained after testing for the condition specified above is completed, to allow testing for other conditions. Testing for other conditions requires written authorization by the patient or an individual authorized to make medical decision for the patient.

6b. I indicate my desire to opt out of having my sample retained for more than sixty days after the sample was taken by checking this box: ☐

7a. After DNA testing is completed, a portion of my sample may be used anonymously for research purposes. Prior to use in research, all identifiers will be removed from a portion of my sample and from my clinical information. I understand that the use of my anonymized sample and clinical information for research purposes may contribute to the identification of new genes, the creation of new diagnostic tests or new medicines, or other events that may be commercially valuable and that I will not receive any financial benefits from such developments.

7b. I indicate my desire to opt out of having my anonymized sample and clinical information used for research purposes by checking this box: ☐. Refusal to permit use of my anonymized sample and clinical information for research purposes will not affect this test procedure.

8. Participation in DNA testing is completely voluntary, and the decision to consent to or to refuse the above testing is entirely mine.

9. My signature below indicates that I have read, or had read to me, the above information and that I understand it. I have had the opportunity to discuss the information, including the purposes and possible risks of genetic testing, with my doctor or someone my doctor has designated. I know that I may obtain professional genetic counseling before signing this consent if I wish. I have all the information I want, and all of my questions have been answered.

Signature __________________________________________ Date ______________________

Printed Name _______________________________________

Witnessed by:

Signature __________________________________________ Printed Name ______________________

Physician/Counselor Statement: I have explained DNA testing to this individual. I have addressed the limitations outlined above, and I have answered the person's questions.

Signature __________________________________________ Date ______________________

Printed Name _______________________________________

Informed Consent 12/08