INHERITED CARDIOMYOPATHIES Requisition

Ship to:
Molecular Genetics Diagnostic Laboratory
Regional Genetics Program
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Ottawa, ON, K1H 8L1
Tel: (613) 738-3230 Fax: (613) 738-4814
http://www.cheo.on.ca/en/moleculargenetics

Patient Name: _____
Last First Initial
Health Card Number: _____
DOB: (yy/mm/dd) _____
Address: _____
_____
Telephone: _____

Gender (circle one): Male ☐ Female ☐

ALL SECTIONS MUST BE COMPLETED

Collection Date: _____ CHEO Pedigree Number: _____
Collection Centre: _____

Sample Requirements

Blood

☐ EDTA (lavender top) _____ mL room temp *(3 ML for infants 1 year or less; otherwise 2 X 5 ML)*

For any other sample types, please contact the laboratory directly.

Health Care Provider Requesting Test

Name: _____
Registration Number: _____
Address: _____
_____
Telephone: _____
FAX: _____

Copy to: Name: _____
Registration Number: _____
Address: _____
_____
Telephone: _____
FAX: _____

Test Requested (see next page for the clinical testing criteria and a list of the genes included in each panel)

□ ARVC panel *(7 genes)*
□ CPVT panel *(2 genes)*
□ DCM panel *(25 genes)*
□ HCM panel *(19 genes)*
□ Pan Cardiomyopathy panel *(45 genes)* ***Note: most appropriate for overlapping or atypical phenotypes. If a disease-specific panel is negative and you would like to reflex to this panel, please contact the laboratory.***
□ Single gene testing (Specify Gene): _____
□ Store DNA for future testing *(DNA will be stored for 2 years then discarded; contact the laboratory directly if a longer storage term is required)*

□ Family Variant Specific Test
(Include a copy of the family member's genetic test report. A positive control is recommended if testing was performed in a different lab)
Gene_____ Variant _____
Gene_____ Variant _____
Gene_____ Variant _____
Proband name: _____
Relationship to proband: _____

Clinical Information

Clinical Diagnosis: □ HCM □ DCM □ ARVC □ CPVT □ LVNC □ RCM □ CHD □ Unknown
□ Unaffected □ Other _____

Cardiovascular Features:

Left Ventricular Hypertrophy □ Asymmetric □ Concentric
Max. LV wall thickness: _____ (mm)
Ventricular Enlargement/Dilation □ Left □ Right
Reduced Ejection Fraction □ Yes ____% □ No
Conduction Disease/Arrhythmia □ WPW □ Ventricular Tachycardia
□ AV Block □ Atrial Fibrillation
□ Other _____

Other Clinical Features:
☐ Yes (specify below) ☐ No ☐ Unknown
_____
_____
_____

Ethnicity: (be as specific as possible)
□ Ashkenazi Jewish □ Black/African □ East Asian □ European □ First Nations □ French Canadian
□ Hispanic □ Middle Eastern □ South Asian □ Other _____

Positive Family History □ Yes (specify below) □ No □ Unknown
_____
_____

INHERITED CARDIOMYOPATHIES TEST DETAILS

Clinical criteria for genetic testing:

1) Patient has a clinical diagnosis of the relevant condition
2) Patient does not have a diagnosis of the relevant condition, but clinical suspicion is strong
3) Patient has a family history of a pathogenic or likely-pathogenic mutation; in this scenario, testing should consist of analysis for the familial mutation only

Methodology of genetic testing:

1) Sequencing: analysis of coding sequences of the relevant genes and 10 base pairs immediately adjacent to each exon. This test is performed by oligonucleotide-based target capture (TruSight Cardiomyopathy Panel, Illumina) followed by next generation sequencing using the MiSeq instrument (Illumina). Additional Sanger sequencing is performed for relevant regions that have insufficient coverage, and to confirm all clinically significant variants and variants of unknown significance.
2) MLPA: to detect large genomic deletions and duplications, multiplex ligation-dependent probe amplification (MLPA) is performed for the relevant genes.

Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC) Panel
Genes included in panel: *DSC2, DSG2, DSP, JUP, PKP2, RYR2,* and *TMEM43*
Analysis includes sequencing as described above, and MLPA of *DSC2, DSG2, DSP* and *PKP2*.

Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT) Panel
Genes included in panel: *CASQ2* and *RYR2*
Analysis includes sequencing as described above.

Hypertrophic Cardiomyopathy (HCM) Panel
Genes included in panel: *ACTC1, ACTN2, CAV3, CSRP3, GLA, LAMP2, MYBPC3, MYH7, MYL2, MYL3, MYOZ2, NEXN, PLN, PRKAG2, TNNC1, TNNI3, TNNT2, TPM1,* and *TTR*
Analysis includes sequencing as described above, and MLPA of *MYH7, MYBPC3* and *TNNT2.*

Dilated Cardiomyopathy (DCM) Panel
Genes included in panel: *ABCC9, ACTC1, ACTN2, CSRP3, CTF1, DES, EMD, LAMP2, LDB3, LMNA, MYBPC3, MYH6, MYH7, NEXN, PLN, RBM20, SGCD, TAZ, TCAP, TNNC1, TNNI3, TNNT2, TPM1, TTN,* and *VCL*
Analysis includes sequencing as described above, and MLPA of *MYH7, MYBPC3* and *TNNT2.*

Pan Cardiomyopathy Panel
Genes included in panel: *ABCC9, ACTC1, ACTN2, ANKRD1, CASQ2, CAV3, CRYAB, CSRP3, CTF1, DES, DSC2, DSG2, DSP, EMD, FHL2, GLA, JUP, LAMA4, LAMP2, LDB3, LMNA, MYBPC3, MYH6, MYH7, MYL2, MYL3, MYLK2, MYOZ2, NEXN, PKP2, PLN, PRKAG2, RBM20, RYR2, SGCD, TAZ, TCAP, TMEM43, TNNC1, TNNI3, TNNT2, TPM1, TTN, TTR,* and *VCL*
Analysis includes sequencing as described above, and MLPA of *DSC2, DSG2, DSP, MYH7, MYBPC3, PKP2* and *TNNT2*.

Frequently Asked Questions about the Pan Cardiomyopathy Panel:

1) When is the pan cardiomyopathy panel appropriate to order (as opposed to a smaller disease-specific panel)?
    - When the patient has cardiomyopathy or strong clinical suspicion of cardiomyopathy, with features overlapping or atypical of conventional disease categories.
    - It is important to note that the pan cardiomyopathy panel is not a comprehensive arrhythmia panel. If the primary etiology is felt to be more likely a channelopathy, a comprehensive arrhythmia panel may be better suited. For instance, if a patient has VF arrest at 40 years or less, without a clear etiology identified, the pan cardiomyopathy panel is likely not the most appropriate first step.
2) Why wouldn't I always order the pan cardiomyopathy panel?
    - Because of the large number of genes analysed, the pan cardiomyopathy panel is likely to yield a higher number of variants of unclear clinical significance than the disease-specific panels. These variants can be difficult for the ordering provider and the patient to interpret.
    - If the patient's disease is consistent with an established cardiomyopathy, an expanded panel is expected to add only limited additional sensitivity [Alfares et al (2015) Genet Med, PMID 25611685].