Cincinnati Children's
Heart Institute

Heart Institute Diagnostic Lab
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CLIA#: 36D2003208
Phone: (513) 803-1751
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Shipping Instructions

Please enclose a test requisition form with sample. All information must be complete before sample can be processed. Samples may be shipped at room temperature by overnight Federal Express to arrive Monday through Friday.

Ship To:

Cincinnati Children's
Hospital Medical Center
Attn: Heart Institute Diagnostic Lab
240 Albert Sabin Way,
Room S4.381
Cincinnati, OH 45229-3039

MYH11 – Familial Thoracic Aortic Aneurysms and Aortic Dissections

Familial Thoracic Aortic Aneurysms and Aortic Dissections (TAAD) is defined as the presence of dilation and/or dissection of the ascending aorta in the absence of any connective tissue abnormalities and in the presence of a positive family history. It is estimated that 20% of thoracic aortic aneurysms and dissections result from a genetic predisposition (1). TAAD has been linked to several genes including *TGFBR1*, *TGFBR2*, *MYH11*, *FBN1*, and *ACTA2*. *MYH11* encodes the protein myosin-11, which is a component of the myosin heavy chain in smooth muscle. Mutations in the *MYH11* gene affect the structure and assembly of the myosin thick filaments and have a dominant negative affect. The *MYH11* gene contains 41 exons and is located on chromosome 16p13.13-p13.12.

Causative mutations can be identified in approximately 18% of individuals with TAAD. Mutations in *ACTA2* account for the majority of cases (14%), while mutations in *TGFBR2* and *TGFBR1* account for 2.5% and 1%, respectively. Mutations in *MYH11* have been identified in 2 families with TAAD, who also presented with patent ductus arteriosus (2). TAAD has an autosomal dominant pattern of inheritance, with decreased penetrance and variable expressivity. Most affected individuals have a parent who is also affected. Aortic aneurysms and dissection can also be associated with genetic syndromes. Before testing the *MYH11* gene it is important to rule out any underlying connective tissue disorders.

Indication

MYH11 gene testing is utilized to confirm a diagnosis of TAAD in patients with clinically evident disease. Genetic testing allows for early identification and diagnosis of individuals at greatest risk prior to the expression of typical clinical manifestations.

Methodology:

All 41 exons of the *MHY11* gene, as well as the exon/intron boundaries and portion of untranslated regions of the gene are amplified by PCR. Genomic DNA sequences from both forward and reverse directions are obtained by automatic fluorescent detection using an *ABI PRISM® 3730 DNA Analyzer*. Sequence variants different from National Center for Biotechnology Information GenBank references are further evaluated for genetic significance. If a mutation is identified, a known familial mutation analysis will be available for additional family members.

Sensitivity & Accuracy:

Greater than 98.5% of the mutations in exons 1-41 of *MYH11* are detectable by sequence based methods. Sequencing does not detect deletions or duplications.

References:

1. Coady MA, Davies RR, Roberts M, Goldstein LJ, Rogalski MJ, Rizzo JA, Hammond GL, Kopf GS, Elefteriades JA. Familial patterns of Thoracic Aortic Aneurysms. *Archives of Surgery*. 1999;134:361-367.

2. Zhu L, Vranckx R, Khau Van Kien P, Lalande A, Boisset N, Mathieu F, Wegman M, Glancy L, Gasc JM, Brunotte F, Bruneval P, Wolf JE, Michel JB, Jeunemaitre X. Mutations in myosin heavy chain 11 cause a syndrome associating Thoracic Aortic Aneurysm/aortic dissection and patent ductus arteriosus. *Nature Genetics*. 2006;38:343-349.

3. Brautbar A, LeMaire SA, Franco LM, Coselli JS, Milewicz DM, Belmont JW. *FBN1* mutations in patients with descending thoracic aortic dissections. *American Journal of Medical Genetics Part A*. 2010;152A:413-416.

Specimen:

Peripheral blood in EDTA tube
Adult: 5-10mL
Child: 3-5mL
Infant: 1-3mL
For other specimen types, please contact Amy Shikany at 513-803-3317

Turnaround Time:

Full Mutation Analysis 4-6 weeks
Known Mutation Analysis 1-2 weeks

CPT Codes:

Full Gene Sequencing	81479
Additional Family Members	81403