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.

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.

Sensitivity & Accuracy:

References:


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