Myosin heavy-chain 11 is a smooth muscle myosin belonging to the myosin heavy-chain family. It is a subunit of a hexameric protein that consists of two heavy-chain subunits and two pairs of non-identical light-chain subunits and functions as a major contractile protein, converting chemical energy into mechanical energy through the hydrolysis of ATP. Myosin heavy-chain 11 is encoded by the \textit{MYH11} gene, which is composed of 41 coding exons and is located at 16p13.13-p13.12. Deletion, splicing and missense mutations in the \textit{MYH11} have been identified in patients with familial thoracic aortic aneurysm/dissection with patent ductus arteriosus type 4 (AAT4), which is one of the most severe cardiovascular conditions in adults. Studies have shown that MYH11 heterozygous mutation leads to an early and severe decrease in the elasticity of the aortic wall consistent with the role of smooth muscle cells in maintaining the mechanical properties of the thoracic aorta. AAT4 demonstrates autosomal dominant inheritance. Definitive genotype/phenotype correlations have not been described.

The John Welsh Cardiovascular Diagnostic Laboratory offers molecular genetic testing for \textit{MYH11} mutations. Individuals are tested by DNA sequencing of the 41 coding exons of the \textit{MYH11} gene. We strongly recommend initial testing of a clearly affected individual, if available, in order to provide the greatest test sensitivity and clearest interpretation of results for subsequent family members. Genetic counseling is recommended for all individuals.

### REASONS FOR REFERRAL
- Molecular confirmation of the diagnosis of familial thoracic aortic aneurysm 4 (AAT4)

### METHODOLOGY

Genomic DNA is analyzed for \textit{MYH11} mutations by DNA sequencing of the 41 coding exons of the \textit{MYH11} gene, as well as the exon/intron junctions and a portion of the 3` untranslated region. Patient DNA is sequenced in both the forward and reverse orientations. If a mutation is identified, additional family members are analyzed only for the familial mutation by automatic fluorescent DNA sequencing.

### SERVICE FEES

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<th>Direct and Institutional Billing</th>
<th>CPT Codes</th>
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<td>Index Case (Male or Female)</td>
<td>$1500 per sample</td>
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<tr>
<td>Additional Family Members</td>
<td>$300 per sample; Known familial mutation only</td>
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### SENSITIVITY

DNA Sequencing Analysis: Approximately 95% detection of mutations in 41 exons of \textit{MYH11}

### SPECIMEN REQUIREMENTS

- **Blood (preferred):** EDTA (purple-top) tubes: \textit{Adult}: 5 cc \textit{Child}: 5 cc \textit{Infant}: 2-3 cc
- **Tissue:** Frozen (preferred), RNA\textit{Later}
- **Other Body Fluids and Formalin-fixed, Paraffin-embedded Tissue:** Call to inquire