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. TAAD has been linked to several genes including TGFBR1, TGFBR2, MYH11, FBN1, and ACTA2. ACTA2 encodes a smooth muscle protein called alpha-actin, which is a major contractile protein in smooth muscle. Mutations in the ACTA2 gene affect both the structure and the assembly of the actin filaments and have a dominant negative affect, leading to impaired contractility. The ACTA2 gene contains 9 exons and is located on chromosome 10q22-q24.

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, TGFBR1, and MYH11 account for 2.5%, 1%, and less than 1%, respectively. TAAD has an autosomal dominant pattern of inheritance. Most affected individuals have a parent who is also affected.

Aortic aneurysms and dissections can also be associated with genetic syndromes. Before testing the ACTA2 gene it is important to rule out any underlying connective tissue disorders.

**Indication**

ACTA2 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 9 exons of the *ACTA2* 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 1-9 of *ACTA2* are detectable by sequence based methods. Sequencing does not detect deletions or duplications.

References:


Specimen:
Peripheral blood in EDTA tube
Adult: 3-5mL
Child: 3-5mL
Infant: 1-3mL
For other specimen types, please contact us at 513-636-4474

Turnaround Time:
Full Mutation Analysis 2-4 weeks
Known Mutation Analysis 1-2 weeks

CPT Codes:
Full Gene Sequencing  81405
Additional Family Members  81403

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