The transforming growth factor-beta family of polypeptides (TGF-β1, TGF-β2 and TGF-β3) is involved in the regulation of cellular processes, including cell division, differentiation, motility, adhesion and death. TGF-beta signals by binding the TGF-beta type II receptor (TGFBR2) which transphosphorylates and activates the type I receptor (TGFBR1). Activated TGFBR1 then phosphorylates a subset of SMAD proteins, SMAD2 and SMAD3, which translocate to the nucleus where they form transcription complexes with DNA binding factors and co-activators/co-repressors.

TGF-β2 is a secreted protein known as a cytokine that performs many cellular functions and has a vital role during embryonic development (alternative names: Glioblastoma-derived T-cell suppressor factor, G-TSF, BSC-1 cell growth inhibitor, Polyergin, Cetermin). It is an extracellular glycosylated protein and known to suppress the effects of interleukin dependent T-cell tumors. There are two named isoforms of this protein, created by alternative splicing of the same gene. The full-length TGFB2 gene contains 8 exons spanning 98.6 kb genomic distance that was mapped to chromosome 1q41. Mutations in the TGFB2 gene cause familial thoracic aortic aneurysms and dissections (TAAD) associated with mild systemic features of Marfan syndrome and Loeys-Dietz syndrome. TGFB2 mutations demonstrate autosomal dominant inheritance with a broad range of clinical severity both within and between families. Definitive genotype/phenotype correlations have not been described.

The John Welsh Cardiovascular Diagnostic Laboratory offers molecular genetic testing for TGFB2 mutations. Individuals are tested by DNA sequencing of the coding exons of the TGFB2 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 thoracic aortic aneurysms and dissections (TAAD), Marfan syndrome (MFS) and Loeys-Dietz syndrome (LDS).

### METHODOLOGY
Genomic DNA will be analyzed for TGFB2 mutations by DNA sequencing of the coding exons of the TGFB2 gene, as well as the exon/intron junctions and a portion of the 5’ and 3’ untranslated region. Patient DNA will be sequenced in both the forward and reverse orientations. If a mutation is identified, additional family members will be analyzed only for the familial mutation by automatic fluorescent DNA sequencing.

### SERVICE FEES

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<th>Direct and Institutional Billing</th>
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<td>Index Case (Male or Female)</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 99 percent detection of mutations in the coding exons 1-8 of TGFB2.

### SPECIMEN REQUIREMENTS

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