Marfan Syndrome, Thoracic Aortic Aneurysm & Dissection (TAAD), and Related Disorders: Sequencing Panel

**Test Code:** MM099  
**Turnaround time:** 6 weeks  
**CPT Codes:** 81410 x1

### Condition Description
Thoracic aortic aneurysm and dissection (TAAD) has a highly variable presentation and age of onset. It is characterized by dilation and dissections of the ascending thoracic aorta and/or ascending aorta. An aneurysm involving the descending thoracic aorta is observed rarely. Without surgical repair of the ascending aorta, individuals with TAAD have continual enlargement of the ascending aorta that leads to an acute aortic dissection. Isolated TAAD is typically inherited in an autosomal dominant manner with variable expression and reduced penetrance. Only about 20% of familial non-syndromic TAAD is attributed to pathogenic variants in known genes.

TAAD can also be present as part of a genetic syndrome. Marfan syndrome, Loeys-Dietz syndrome, Ehlers-Danlos syndrome vascular type, multisystemic smooth muscle dysfunction syndrome, and congenital contractural arachnodactyly all have TAAD as part of their clinical spectrum.


### References:
- GeneReviews
- OMIM

### Genes
- ACTA2, CBS, COL3A1, COL5A1, COL5A2, FBN1, FBN2, FLNA, MED12, MYH11, MYLK, SKI, SLC2A10, SMAD3, TGFBR1, TGFBR2

### Indications
This test is indicated for:
- Confirmation of a clinical diagnosis of thoracic aortic aneurysm and dissection (TAAD).
- Confirmation of a clinical diagnosis of Marfan syndrome.

### Methodology
**Next Generation Sequencing:** In-solution hybridization of all coding exons is performed on the patient's genomic DNA. Although some deep intronic regions may also be analyzed, this assay is not meant to interrogate most promoter regions, deep intronic regions, or other regulatory elements, and does not detect single or multi-exon deletions or duplications. Direct sequencing of the captured regions is performed using next generation sequencing. The patient's gene sequences are then compared to a standard reference sequence. Potentially causative variants and areas of low coverage are Sanger-sequenced. Sequence variations are classified as pathogenic, likely pathogenic, benign, likely benign, or variants of unknown significance. Variants of unknown significance may require further studies of the patient and/or family members.

### Detection
**Next Generation Sequencing:** Clinical Sensitivity: Only about 20% of familial non-syndromic TAAD is attributed to pathogenic variants in known genes. It is unknown for syndromic forms of TAAD. Pathogenic variants in the promoter region, some pathogenic variants in the introns and other regulatory element pathogenic variants cannot be detected by this analysis. Large deletions will not be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's clinical and/or biochemical phenotype.

**Analytical Sensitivity:** ~99%.

### Specimen Requirements
**Submit only 1 of the following specimen types**

#### Type: DNA, Isolated

**Specimen Requirements:**
Microtainer
8µg
Isolation using the PerkinElmer™Chemagen™ Chemagen™ Automated Extraction method or Qiagen™ Puregene kit for DNA extraction is recommended.

**Specimen Collection and Shipping:**
Refrigerate until time of shipment in 100 ng/µL in TE buffer. Ship sample at room temperature with overnight delivery.

#### Type: Saliva

**Specimen Requirements:**

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Oragene™ Saliva Collection Kit
Oragene™ Saliva Collection Kit used according to manufacturer instructions. Please contact EGL for a Saliva Collection Kit for patients that cannot provide a blood sample.

**Specimen Collection and Shipping:**
Please do not refrigerate or freeze saliva sample. Please store and ship at room temperature.

**Type: Whole Blood (EDTA)**

**Specimen Requirements:**
- EDTA (Purple Top)
- Infants and Young Children (2 years of age to 10 years old): 3-5 ml
- Older Children & Adults: 5-10 ml
- Autopsy: 2-3 ml unclotted cord or cardiac blood

**Specimen Collection and Shipping:**
Ship sample at room temperature for receipt at EGL within 72 hours of collection. Do not freeze.

**Related Tests**
- Comprehensive cardiomyopathy panel
- Marfan Syndrome, Thoracic Aortic Aneurysm & Dissection (TAAD), and Related Disorders: Deletion/Duplication Panel