

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

**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.

Visit [www.ThinkGenetic.com](http://www.ThinkGenetic.com) for patient-friendly information on [Marfan syndrome](#).

References:

- GeneReviews
- OMIM

### Genes

[ACTA2](#), [CBS](#), [COL3A1](#), [COL5A1](#), [COL5A2](#), [FBN1](#), [FBN2](#), [FLNA](#), [MED12](#), [MYH11](#), [MYLK](#), [SKI](#), [SLC2A10](#), [SMAD3](#), [TGFB2](#), [TGFB1](#), [TGFB2](#)

### 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.

**Copy Number Analysis:** Comparative analysis of the NGS read depth (coverage) of the targeted regions of genes on this panel was performed to detect copy number variants (CNV). The accuracy of the detected variants is highly dependent on the size of the event, the sequence context and the coverage obtained for the targeted region. Due to these variables and limitations a minimum validated CNV size cannot be determined; however, single exon deletions and duplications are expected to be below the detection limit of this analysis.

### 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. Results of molecular analysis should be interpreted in the context of the patient's clinical and/or biochemical phenotype.

Analytical sensitivity for sequence variant detection is ~99%.

**Copy Number Analysis:** The sensitivity and specificity of this method for CNV detection is highly dependent on the size of the event, sequence context and depth of coverage for the region involved. The assay is highly sensitive for CNVs of 500 base pairs or larger and those containing at least 3 exons. Smaller (< 500 base pairs) CNVs and those that involving only 1 or 2 exons may or may not be detected depending on the sequence context, size of exon(s) involved and depth of coverage.

### Specimen Requirements

*Submit only 1 of the following specimen types*

**Type:** DNA, Isolated

**Specimen Requirements:**

Microtainer

8µg

Isolation using the Perkin Elmer™ 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:**

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