Connective Tissue Disorders: Sequencing Panel

**Condition Description**

Connective tissues provide a framework and structural support for the body, protect organs, connect body tissues, and store energy. Connective tissue disorders are a heterogeneous group of more than 200 conditions that often involve the joints, muscles, and skin. Heritable connective tissue disorders include both soft tissue disorders, characterized by excessive skin laxity, joint hypermobility, and easy bruising, as well as skeletal dysplasias that affect bone development.

Diagnosis of heritable connective tissue disorders may be challenging due to extensive clinical variability, phenotypic overlap, or atypical presentation. However, making a specific diagnosis is important given that some of these disorders feature life-threatening complications, such as aortic root rupture, that require careful medical surveillance and monitoring. In addition, treatment options are available for some connective tissue disease.

**Reference:**
- Bateman et al. (2009), Nat Rev Genet. 10:173-183.

**Genes**

ACTA2, ACVR1, ADAMTS2, ATP6V0A2, CBS, CHST14, COL1A1, COL1A1, COL1A2, COL2A1, COL3A1, COL5A1, COL5A2, ELN, FBLN5, FBN1, FBN2, FKBP14, MYLK, NOTCH1, PKD2, PLOD1, PRDM5, SLC2A10, SLC39A13, SMAD3, TGFBR1, TGFBR2, ZNF469

**Indications**

This test is indicated for:
- Confirmation of a clinical diagnosis of connective tissue disorder.

**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: Unknown. Pathogenic variants in the promoter region, some pathogenic variants in the introns and other regulatory element mutations cannot be detected by this analysis. Large deletions/duplications will not be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's clinical/biochemical phenotype.

Analytical Sensitivity: ~99%.

**Specimen Requirements**

Submit only 1 of the following specimen types

**Type: Whole Blood**

Specimen Requirements:
- In EDTA (purple top) tube:
  - Infants (2 years): 3-5 ml
  - Older Children & Adults: 5-10 ml

Specimen Collection and Shipping: Ship sample at room temperature with overnight delivery.

**Type: Isolated DNA**

Specimen Requirements:
- In microtainer: 60 ug

Isolation using the Qiagen™ Puregene kit for DNA extraction is recommended.
Specimen Collection and Shipping: Refrigerate until time of shipment in 100 ng/ul of TE buffer. Ship sample at room temperature with overnight delivery.

**Related Tests**

- Connective Tissue Disorders: Deletion/Duplication Panel