PREVENTION GENETICS
DISEASE PREVENTION THROUGH GENETIC TESTING

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Stickler Syndrome, Type I (STL1) via *COL2A1* Gene Sequencing (Test #788)

Brief Description of Clinical Features: Stickler syndrome is a multisystem connective tissue disorder that can include ocular findings of myopia, cataract, and retinal detachment; hearing loss that is both conductive and sensorineural; midfacial underdevelopment and cleft palate (either alone or as part of the Robin sequence); and mild spondyloepiphyseal dysplasia and/or precocious arthritis (Robin et al. *GeneReview*, 2010). At present, at least three types of autosomal dominant and one type of autosomal recessive Stickler syndrome have been described. The majority (80-90%) of individuals with Stickler syndrome have Type I or "membranous" (OMIM#108300), characterized by a persistence of vestigial vitreous gel in the retrolental space.

Genetics: STL1 is inherited in an autosomal dominant manner and caused by mutation in the *COL2A1* gene. *COL2A1* encodes the alpha 1 chain of type II collagen, a major structural component of cartilaginous tissues. The majority (>90%) of STL1-associated *COL2A1* mutations are truncating mutations resulting in haploinsufficiency of type II collagen (Hoornaert et al. *Eur J Hum Genet* 18:827-881, 2010). Mutations in *COL2A1* can also cause several other skeletal disorders, including Achondrogenesis type II/Hypochondrogenesis (OMIM#200610), Spondyloepiphyseal dysplasia congenita (OMIM#183900), Spondyloepimetaphyseal dysplasia, Strudwick type (OMIM#184250), Spondyloperipheral dysplasia (OMIM#271700), Kniest dysplasia (OMIM#156550), Osteoarthritis with mild chondrodysplasia (OMIM#604864), and Platyspondylic lethal skeletal dysplasia, Torrance type (OMIM#151210).

Description of This Particular Test: This test involves bidirectional sequencing using genomic DNA of all coding exons of the *COL2A1* gene plus ~50 bp of flanking non-coding DNA on each side. As indicated, we will also sequence any single exon (Test #100, $190) in family members of patients with a known mutation, or to confirm research results.

Reference Sequences: **Genomic: NC_000012.11** **mRNA: NM_001844.4**
Protein: NP_001835.3 **mRNA and Protein: CCDS 41778.1**

Indications for Test: Candidates for this test are patients with clinical features consistent with STL1, and family members of patients who have a known *COL2A1* mutation.

Sensitivity of Test: This test is predicted to detect disease mutations in ~90% of individuals with a clinical diagnosis of STL1 (Robin et al. *GeneReview*, 2010).

Turnaround Time: Maximum of 40 calendar days, although many tests are completed in 2-3 weeks.

Specimen Requirements: See page four of the Requisition Form.

Prices: **Sequencing of *COL2A1* gene** **$ 1990**

CPT Codes:

Sample Ascertainment x1	83890 $ 30	DNA Isolation x1	83891 $ 40
Amplification x47	83898 $660	Sequencing x47	83904 $990
Separation x1	83894 $140	Interpretation/Report x1	83912 $130

Accreditation: CLIA ID #: 52D1027685 (expires 1/18/13) (CAP#: 7185561, AU ID: 1407125 expires 12/20/12).

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