

Kniest Dysplasia via COL2A1 Gene Sequencing (Test #788)

Brief Description of Clinical Features: Kniest dysplasia (OMIM#156550) is a moderately severe type II collagenopathy, characterized by short-trunk dwarfism with kyphoscoliosis, prominent joints, midface hypoplasia, prominent eyes, cleft palate, hearing loss, myopia, and/or retinal detachment (Gilbert-Barnes et al. *Am J Med Genet* 63:34-45, 1996).

Genetics: Kniest dysplasia is inherited in an autosomal dominant manner. It is caused by mutations in *COL2A1* gene. *COL2A1* encodes the alpha 1 chain of type II collagen, a major structural component of cartilaginous tissues. *COL2A1* mutations can also cause several other skeletal disorders, including Achondrogenesis type II/Hypochondrogenesis (OMIM#200610), Stickler dysplasia type I (OMIM#108300), Spondyloepiphyseal dysplasia congenita (OMIM#183900), Spondyloepimetaphyseal dysplasia Strudwick type (OMIM#184250), Spondyloperipheral dysplasia (OMIM#271700), Osteoarthritis with mild chondrodysplasia (OMIM#604864), and Platyspondylic lethal skeletal dysplasia, Torrance type (OMIM#151210). Most reported Kniest dysplasia-associated *COL2A1* mutations are small, in-frame deletions within coding exons and splice site mutations that cause exon skipping (Wilkin et al. *Am J Med Genet* 85:105-112, 1999).

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) in family members of patients with a known mutation, or to confirm research results (\$190).

Reference Sequences: Genomic: NC_000012.11
Protein: NP_001835.3

mRNA: NM_001844.4
mRNA and Protein: CCDS 41778.1

Indications for Test: Candidates for this test are patients with clinical and radiographic findings consistent with Kniest dysplasia and family members of patients who have a known *COL2A1* mutation.

Sensitivity of Test: Kniest dysplasia is a rare condition. Series of Kniest dysplasia patients screened for *COL2A1* mutations have not been described in the literature. Our test has been designed to detect >99% of mutations published to date.

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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