

Spondyloepiphyseal Dysplasia, Congenita (SEDC) and Spondylometaphyseal dysplasia, Strudwick type (SEMD) via COL2A1 Gene Sequencing (Test #788)

Brief Description of Clinical Features: Spondyloepiphyseal dysplasia congenita (OMIM#183900) is a variable disorder but is evident at birth. Individuals have short trunk and neck, large head, marrow chest, short extremities, and club feet (Turner et al. *Fetal Pediatr Pathol*.29:57-62, 2010). The spine is involved. Myopia and retinal detachment may occur. Spondylometaphyseal dysplasia, Strudwick type (OMIM#184250) is characterized by disproportionate short stature, pectus carinatum, scoliosis, and dapple metaphyses (Tiller et al. *Am J Hum Genet* 11: 87-89, 1995). SEMD is indistinguishable from SEDC at birth, however, more pronounced metaphyseal involvement is evident by childhood.

Genetics: SEDC and SEMD are inherited in an autosomal dominant manner. *COL2A1* is the only gene known to be associated with these two conditions. *COL2A1* encodes the alpha 1 chain of type II collagen, a major structural component of cartilaginous tissues. The majority of SEDC/SEMD-associated *COL2A1* mutations are missense mutations exerting dominant negative effects through the assembly of abnormal alpha I chains into trimeric collagen molecules (Nishimura et al. *Hum Mutat* 26:36-43, 2005). *COL2A1* mutations can also cause several other skeletal disorders, including Achondrogenesis type II/Hypochondrogenesis (OMIM#200610), Stickler dysplasia type I (OMIM#108300), 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 and radiographic findings consistent with SEDC or SEMD, and family members of patients who have a known *COL2A1* mutation.

Sensitivity of Test: This test is predicted to detect disease mutations in >80% of individuals with a clinical diagnosis of SEDC (Nishimura et al. *Hum Mutat* 26:36-43, 2005). SEMD is a rare condition. Series of SEMD patients screened for *COL2A1* mutations have not been described in the literature. Our test has been designed to detect >99% of SEMD 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).

Contact: Dr. Ying Wang, ying.wang@preventiongenetics.com, www.preventiongenetics.com