

## Spondylo-Meta-Epiphyseal Dysplasia, Short Limb-Hand Type (SMED-SL) via *DDR2* Gene Sequencing (Test #625)

**Brief Description of Clinical Features:** Spondylo-meta-epiphyseal dysplasia with short limb and abnormal calcification (SMED-SL; OMIM 271665) is a growth disorder characterized by disproportionate short stature, short limbs, short broad fingers, abnormal metaphyses and epiphyses, platyspondyly and premature calcifications (Borochowitz et al. Am J Med Genet 45:320-326, 1993; Langer et al. Am J Med Genet 45:488-500, 1993; Bargal et al. Am J Hum Genet 84:80-84, 2009; Ali et al. Hum Mol Genet 19:2239-2250, 2010). Additional findings include a short nose with wide nasal bridge and wide nostrils, a long philtrum, ocular hypertelorism, retro/micrognathia, and a narrow chest (Borochowitz et al. 1993; Langer et al. 1993).

**Genetics:** Spondylo-meta-epiphyseal dysplasia with short limb and abnormal calcification is an autosomal recessive disorder caused by mutations in the *DDR2* gene (Bargal et al. 2009). The *DDR2* gene encodes a cell-surface receptor known as discoidin domain receptor 2 (DDR2), a member of the receptor tyrosine kinase family (Bargal et al. 2009). The DDR2 receptor is mainly expressed in mesenchymal cells and consists of extracellular domains, including the discoidin domain and the stalk domain, and intracellular domains including the juxtamembrane domain and the cytosolic tyrosine kinase domain (Ali et al. 2010). The binding of the discoidin domain of the DDR2 receptor to fibrillar collagen is crucial for the activation of the tyrosine kinase signal transduction (Bargal et al. 2009; Ali et al. 2010). The DDR2 receptor has an important role in fundamental processes including cell proliferation, adhesion and migration as well as extracellular matrix remodeling (Ali et al. 2010). A mix of missense and splicing mutations have been reported in *DDR2* gene (Bargal et al. 2009; Ali et al. 2010).

**Description of This Particular Test:** This test involves bidirectional sequencing using genomic DNA of the 16 coding exon (exons 4-19) of the *DDR2* gene. The full coding region of each exon plus ~50 bp of flanking non-coding DNA on each side are sequenced. As indicated, we will also perform sequencing of any single exon (Test #100) or pair of exons (Test #200) for family members of patients with known mutations and to confirm previous research results (\$190-340 charge).

**Reference Sequences:** Genomic: NC\_000001.10 mRNA: NM\_006182.2 Protein: NP\_006173.2 (CCDS 1241.1)

**Indications for Test:** Candidates for this test are patients with symptoms consistent with Spondylo-meta-epiphyseal dysplasia with short limb and family members of patients who have known *DDR2* mutations.

**Sensitivity of Test:** The prevalence of the *DDR2* mutations is currently unknown.

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

**Specimen Requirements:** See page 4 of the Requisition Form.

**Prices:**                      **Sequencing of *DDR2* gene**    **\$ 910**

**CPT Codes:**

Sample Ascertainment x1	83890 \$ 30	DNA Isolation x1	83891 \$ 40
Amplification x16	83898 \$ 260	Sequencing x16	83904 \$ 400
Separation x1	83894 \$ 70	Interpretation/Report x1	83912 \$ 110

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

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