

Spondylocostal Dysostosis Testing via *DLL3* Exon Sequencing (Test #421)

Brief Description of Disorder: Spondylocostal Dysostosis (SCD) (OMIM 277300, 608681, 609813) is characterized by abnormal segmentation of the vertebral column. Patients have short trunks with multiple vertebral defects and rib anomalies (Turnpenny et al. J Med Genet 40:333-339, 2003). An autosomal dominant and three autosomal recessive forms (Types 1-3) of SCD are known. The most common recessive type (Type 1) is caused by mutations in the delta-like 3 (*DLL3*) gene.

Genetics: SCD, Type 1 is an autosomal recessive disorder. Responsible mutations were identified in the *DLL3* gene on chromosome 19 (Bulman et al. Nature Genet 24:438-441, 2000). About 25 different causative *DLL3* mutations have been reported. Although some are missense, the great majority are nonsense, splicing, and particularly, frameshift. Mutations are located throughout the length of the gene. No mutations are predominant. The genes responsible for recessive SCD, Type 2 (*MESP2*) and Type 3 (*LFNG*) have been identified, but to date only one causative mutation has been reported in each of these genes. Insufficient cases have yet been studied to make firm conclusions about phenotypic differences among the three types.

Description of This Particular Test: This test involves bidirectional DNA sequencing of the coding regions of all 8 exons of *DLL3* plus about 50 bp of flanking non-coding DNA on each side. Sequencing of *MESP2* and *LFNG* genes is also available from PreventionGenetics.

Indications for Test: All SCD patients are candidates for this test. We offer sequencing of one or two exons in parents and other family members of patients with known mutations. We also offer clinical confirmation of mutations that have been identified in research labs.

Sensitivity of Test: Sparrow et al. (Am J Hum Genet 78:28-37, 2006) reported that 20-25% of SCD patients have mutations in *DLL3*. *DLL3* mutations appear to be by far the most common, known cause of SCD.

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

SPECIMEN REQUIREMENTS: See page 4 of the Requisition Form.

Sequencing of the 8 coding exons of the *DLL3* gene **\$590.**

Sample Ascertainment		83890	\$ 30
DNA Isolation		83891	\$ 30
Amplification	x 9	83898	\$160
Mutation Identification by Sequencing	x 9	83904	\$240
Interpretation and Report		83912	\$130

Single exon sequencing for the presence of previously identified mutations in the *DLL3* gene is also available for \$190, or two exon sequencing for \$340.

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

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