

Dentinogenesis Imperfecta (DGI) and Dentin Dysplasia (DD) via *DSPP* Gene Sequencing (Test #771)

Brief Description of Clinical Features: Inherited dentin malformations are classified into three types of dentinogenesis imperfecta (DGI) and two types of dentin dysplasia (DD) (Shields et al. *Archives of Oral Biology* 18:543-553, IN7, 1973).

DGI-I (OMIM 166240): Syndromic DGI. This includes individuals afflicted with osteogenesis imperfecta. Both deciduous and permanent teeth are discolored (grey-yellowish) and worn. Pulpal obliteration is apparent both prior to and upon tooth eruption. Expressivity is variable, even within a single patient, ranging from total obliteration to normal-appearing dentin.

DGI-II (OMIM 125490): Similar to DGI-I, but penetrance is almost complete and expressivity is consistent.

DGI-III (OMIM 125500): Phenotypic variant of DGI-II, but with large pulp chambers resembling shell teeth in deciduous teeth.

DD-I (OMIM 125400): Deciduous and permanent teeth appear normal, but radiologically show short roots with crescent-shaped pulpal remnant parallel to the cemento-enamel junction in the permanent teeth and total pulpal obliteration in the deciduous teeth. Non-carious teeth usually show numerous periapical radiolucencies.

DD-II (OMIM 125420): Deciduous teeth have features of DGI-II. The permanent teeth are normal, but pulp cavities show a thistle-tube deformity and commonly contain pulp stones.

Genetics: DGI (opalescent dentin) is the most common heritable dentin disease. In the United States, the prevalence is estimated between 1:6,000 and 1:8,000; DGI-III may be even more predominant in the “Brandywine isolate” population of mixed Caucasian, Black, and Amerindian (see Acevedo et al. *Cells Tissues Organs (Print)* 189:230-236, 2009). Mutations in the *DSPP* gene are known to cause DGI-II (Xiao et al. *Nat Genet* 27:201-204, 2001; Malmgren et al. *Hum Genet* 114:491-498, 2004), DGI-III (Dong et al. *Am J Med Genet* 132A:305-309, 2005; Kim et al. *Hum Genet* 116:186-191, 2005), and DD-II (Rajpar et al. *Hum Mol Genet* 11:2559-2565, 2002). Mutations in *DSPP* exhibit an autosomal dominant mode of inheritance. *DSPP* encodes a 940 amino-acid polypeptide produced in odontoblasts that is cleaved into dentin sialoprotein (DSP) and dentin phosphoprotein (DPP) (MacDougall et al. *J Biol Chem* 272:835-842, 1997). DSP and DPP are noncollagenous matrix proteins that play a crucial role in dentinogenesis: most causative mutations have been reported in the DSP-coding region (mainly in exons 2-3). Causative mutations are distributed rather evenly among missense / nonsense, splicing, and small deletions. The DGI phenotype is also a variable feature in many other syndromes including Osteogenesis Imperfecta (OI) and Ehlers-Danlos syndrome (EDS), Goldblatt syndrome (OMIM 184260), and Schimke immuno-osseous dysplasia (SIOD, OMIM 242900).

Description of This Particular Test: This test involves complete bidirectional DNA sequencing of coding exons 2-4 of *DSPP* plus ~50 bp of flanking non-coding DNA on either side of each exon. Exon 5 of the gene has a large repeat element; sequencing covers the 5’ portion of the coding sequence up to the repeat and the 3’ portion after the repeat along with ~50 bp of flanking non-coding DNA on either side of this exon. 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_000004.11 mRNA: NM_014208.3 Protein: NP_055023.2 (CCDS 43248.1)

Indications for Test: Patients with symptoms of DGI / DD, and patients with a history of early tooth loss.

Sensitivity of Test: No disease-causing mutations outside of the *DSPP* gene have been identified for nonsyndromic DGI or DD.

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.

Price: Sequencing of *DSPP* \$ 570

CPT Codes							
Test	83890 x1	83891 x1	83898 x8	83904 x8	83894 x1	83912 x1	Total
<i>DSPP</i>	\$30	\$40	\$150	\$230	\$30	\$90	\$570

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

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