

Cranioectodermal Dysplasia 1 (CED1) via *IFT122* Gene Sequencing (Test #623)

Brief Description of Clinical Features: Cranioectodermal dysplasia 1, also known as Sensenbrenner syndrome (CED1; OMIM 218330) is characterized by craniofacial, skeletal and ectodermal anomalies (Levin et al. J Pediat 90:55-61, 1977; Young J Med Genet 26:393-396, 1989; Eke et al. Br J Ophthalmol 80:490-491, 1996; Konstantinidou et al. A J Med Genet 149A:2206-2211, 2009; Walczak-Sztulpa et al. Am J Hum Genet 86:949-956, 2010). CED1 patients demonstrate high degree of phenotypic variations. CED1 dysmorphic features noticed at birth include short limbs, short-narrow thorax, brachydactyly, dolichocephaly, prominent forehead, telecanthus, broad nasal bridge, low-set prominent ears, sparse hair, widely spaced teeth and abnormal nails (Levin et al. 1977; Young 1989; Eke et al. 1996; Walczak-Sztulpa et al. 2010). Other clinical features noticed at early childhood include end-stage renal failure and cardiac anomalies. In addition, a few patients had electroretinographic abnormalities (Eke et al. 1996). Of note, CED1 patients have normal psychomotor development and normal intelligence (Young 1989; Eke et al. 1996; Walczak-Sztulpa et al. 2010).

Genetics: CED1 is inherited in an autosomal recessive manner. Mutations in the *IFT122* gene cause Cranioectodermal dysplasia 1 (Walczak-Sztulpa et al. 2010). *IFT122* gene encodes the IFT122 protein, which contains seven WD40 domains forming the β -propeller structures important for protein-protein interaction (Orlicky et al. Cell 112:243-256, 2003; Walczak-Sztulpa et al. 2010). The IFT122 protein is a component of the intraflagellar transport complex A, which is involved in the retrograde ciliary transport, an important process for cilia assembly and maintenance (Tsao et al. J Cell Sci 121:428-436, 2008; Pedersen and Rosenbaum. Curr Top Dev Biol 85:23-61, 2008; Walczak-Sztulpa et al. 2010). Three missense mutations and one splicing mutation within the *IFT122* gene have been reported (Walczak-Sztulpa et al. 2010).

Description of This Particular Test: This test involves bidirectional sequencing using genomic DNA of the 31 coding exons (exons 1-31) of the *IFT122* 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_000003.11 **mRNA:** NM_052985.1
Protein: NP_443711.1 **mRNA and Protein:** CCDS 3060.1

Indications for Test: Candidates for this test are patients with symptoms consistent with Cranioectodermal dysplasia 1 and family members of patients who have known *IFT122* mutations.

Sensitivity of Test: Sensitivity of this test 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 *IFT122* gene** **\$ 1,460**

CPT Codes:

Sample Ascertainment x1	83890 \$ 30	DNA Isolation x1	83891 \$ 40
Amplification x31	83898 \$ 470	Sequencing x31	83904 \$ 700
Separation x1	83894 \$ 90	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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