

**Leber Congenital Amaurosis, Progressive, via RDH12 Gene Sequencing --Test #821**

**Brief Description of Disorder:** Nonsyndromic Leber Congenital Amaurosis (LCA, OMIM 204000) is a group of severe retinal dystrophies with early onset. The clinical hallmarks are bilateral congenital blindness, a diminished or absent electroretinogram and high hyperopia. Additional symptoms include nystagmus, photophobia, eye poking and sluggish pupils (Cremers et al. Hum Mol Genet 11:1169-1176, 2002). LCA affects 3 per 100,000 newborn babies worldwide and has been described in various ethnic groups. Patients with LCA represent ~ 5% of all retinal dystrophies (Perrault et al. Mol Gen Metabol 68:200-208, 1999). Genetic abnormalities are the primary cause of LCA. See also Weleber et al. (GeneReviews, 2010, [www.genetests.org](http://www.genetests.org)) and the Foundation Fighting Blindness ([www.ffb.ca](http://www.ffb.ca)).

**Genetics:** LCA represents the most common genetic cause of congenital visual impairments in infants and adolescents. It is usually inherited in an autosomal recessive manner, although in several families LCA is transmitted as an autosomal dominant trait (Rivolta et al. Hum Mutat 18:488-498, 2001). Sporadic patients with LCA were also reported (Hanein et al. Hum Mutat 23:306-317, 2004). LCA is genetically and clinically heterogeneous. Currently, mutations in fourteen genes account for ~70% of all cases (den Hollander et al. Prog Retin Eye Res 27:391-419, 2008). The phenotype of LCA patients with *RDH12* mutations may be distinguished by a progressive course and absence or mild hyperopia, suggesting a possible genotype-phenotype correlation (Perrault et al. Am J Hum Genet 75:639-646, 2004). The *RDH12* gene encodes a retinol dehydrogenase, which is expressed predominantly in the neuroretina and involved in the visual cycle. Over 40 different *RDH12* mutations have been reported to date. They include missense, nonsense, splicing, and small deletions. Both homozygous and compound heterozygous mutations have been reported. In addition to LCA, *RDH12* mutations were found in patients with autosomal recessive, childhood-onset severe retinal dystrophy (Janecke et al. Nat Genet 36: 850-854, 2004). More recently, a heterozygous frameshift mutation (c.776delG) was documented as causative for autosomal dominant retinitis pigmentosa characterized by a late onset and relatively mild severity (Fingert et al. Arch Ophthalmol 126:1301-1307, 2008).

**Description of This Particular Test.** This test involves bidirectional DNA sequencing of all coding exons and splice sites of the *RDH12* gene. The full coding sequence of each exon plus ~ 50 bp of flanking-coding DNA on either side are sequenced. As indicated, we will sequence one (Test #100, \$190) or two (Test #200, \$340) exons in family members of patients with known mutations or to confirm previous results.

**Reference Sequences:** Genomic: NC\_000014.8 mRNA: NM\_152443.2 Protein: NP\_689656.2 (CCDS 9787.1)

**Indications for Test:** Patients with LCA and progressive course. *RDH12* is also candidate for patients with other forms of severe retinal dystrophies and patients with AD-RP and no mutations in the genes commonly mutated in patients affected with these conditions.

**Sensitivity of Test:** This test allows the detection of mutations in ~ 4% of patients with LCA (Perrault 2004).

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

**Specimen Requirements and Shipping Instructions:** See page 4 of Requisition Form.

**Price:** Sequencing of all coding exons of the *RDH12* gene: \$ 570

**CPT Codes:**

Sample Ascertainment x1	83890 \$ 30	DNA Isolation x1	83891 \$ 40
Amplification x7	83898 \$ 150	Sequencing x7	83904 \$ 230
Separation x1	83894 \$ 30	Interpretation/Report x1	83912 \$ 90

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

**Contact:** Dr. Khemissa Bejaoui, [khemissa@preventiongenetics.com](mailto:khemissa@preventiongenetics.com), [www.preventiongenetics.com](http://www.preventiongenetics.com)