PREVENTION GENETICS
DISEASE PREVENTION THROUGH GENETIC TESTING

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Leber Congenital Amaurosis or Retinitis Pigmentosa
via RPE65 Gene Sequencing--Test #682

Brief Description of Disorders: Leber Congenital Amaurosis (LCA, OMIM 204100) and Retinitis Pigmentosa (RP, OMIM 268000) are inherited degenerative diseases of the retina. LCA is characterized by bilateral congenital blindness. RP is characterized by night blindness, with age of onset varying from childhood to middle age, and progressing to constriction of the peripheral visual field and, eventually, to loss of central vision. Several clinical features of LCA overlap with those of RP. These include attenuated retinal vessels, abnormal electroretinographic (ERG) findings and a variable amount of retinal pigmentation (Perrault et al. Nat Genet 14:461-464, 1996; Daiger et al. Arch Ophthalmol 125:151-158, 2007; Gu et al. J Med Genet 36:705-707, 1999). Both LCA and RP are clinically and genetically heterogeneous. For additional information see Weleber et al. GeneReviews, 2006 at www.genetests.org.

Genetics: LCA is inherited as an autosomal recessive trait in the vast majority of patients, while RP is either sporadic or familial with various modes of Mendelian, mitochondrial or digenic inheritance. To date, 14 and 25 genes have been implicated in LCA and autosomal recessive RP (AR-RP), respectively (den Hollander et al. Prog Retin Eye Res 27:391-419, 2008; Daiger et al. Arch Ophthalmol 125:151-158, 2007). The clinical overlap between LCA and RP is illustrated by the involvement of six genes in both conditions. These include the *RPE65* gene (Marlhens et al. Nat Genet 17:139-141 1997; Gu et al. Nat Genet 17:194-197, 1997). About 27 and 31 different *RPE65* mutations have been reported in patients with LCA2 (OMIM 204100) and RP20 (OMIM 180069), respectively. The *RPE65* mutations include missense, nonsense, splicing, and small deletions/insertions; they are distributed throughout the entire coding region.

Description of This Particular Test. The RPE65 protein is specifically expressed in the retinal pigment epithelium and is involved in the regeneration of visual pigments. This test involves bidirectional DNA sequencing of all 14 coding exons and splice sites of the *RPE65* gene. The full coding sequence of each exon plus ~ 50 bp of flanking DNA on either side are sequenced. We will sequence any single or double exons in family members of patients with known mutations or to confirm results.
Reference Sequences: Genomic**: NC_000001.9** mRNA and protein: **CCDS 643.1**

Indications for Test: Patients with LCA and AR-RP are candidates.

Sensitivity of Test: RPE65 mutations account for ~ 16 % of patients with LCA and ~ 2 % of patients with AR-RP (Morimura et al. Proc Natl Acad Sci USA 95:3088-3093, 1998).

Turn Around Time: Maximum of 40 calendar days.

Specimen Requirement: See page 4 of the Requisition Form.

Price: **Sequencing of all coding exons of the *RPE65* gene:** **$ 840**

CPT Codes:

Sample Ascertainment x1	83890	$ 30	DNA Isolation x1	83891	$ 40
Amplification x 14	83898	$ 240	Sequencing x 14	83904	$ 370
Separation x1	83894	$ 70	Interpretation/Report x1	83912	$ 90

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

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