

Retinitis Pigmentosa and Leber Congenital Amaurosis via TULP1 Gene Sequencing--Test #683

Brief Description of Disorders: Retinitis Pigmentosa (RP, OMIM 268000) and Leber Congenital Amaurosis (LCA, OMIM 204000) are inherited degenerative diseases of the retina. 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. LCA is characterized by bilateral congenital blindness. 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, and the diagnostic boundary separating autosomal recessive RP (AR-RP) and LCA is not clear (Rivolta et al. Hum Mol Genet 11:1219-1227, 2002). For additional information see Weleber et al. GeneReviews, 2006 at www.genetests.org and the Foundation Fighting Blindness at www.ffb.ca.

Genetics: RP is either sporadic or familial with various modes of Mendelian, mitochondrial or digenic inheritance. Autosomal recessive (AR-RP) is the most severe form of the disease. LCA is inherited as an autosomal recessive trait in the vast majority of patients. To date, 25 and 14 genes have been implicated in AR-RP and LCA, respectively (Daiger et al. Arch Ophthalmol 125:151-158, 2007; den Hollander et al. Prog Retin Eye Res 27:391-419, 2008). The clinical overlap between AR-RP and LCA is illustrated by the involvement of six genes in both conditions. These include the *TULP1* gene (Hagstrom et al. Nat Genet 18:174-176, 1998; Banerjee et al. Nat Genet 18:177-179, 1998). Over 23 different *TULP1* mutations have been reported in patients with AR-RP (RP14, OMIM 600132) including missense, nonsense, splicing, and small deletions/insertions. AR-RP patients with *TULP1* mutations presented with a severe phenotype and variable age of onset. Four *TULP1* mutations were identified in three patients with LCA (OMIM 204000). One patient was compound heterozygote for a splice mutation and a nonsense mutation, and the other two were homozygous for two distinct nonsense mutations (Hanein et al. Hum Mutat 23:306-317, 2004).

Description of This Particular Test. The TULP1 protein is primarily expressed in the retina. This test involves bidirectional DNA sequencing of all 15 coding exons and splice sites of the *TULP1* 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_000006.10** mRNA and protein: **CCDS 4807.1**

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

Sensitivity of Test: TULP1 mutations account for up to 2 % of all AR-RP patients (den Hollander et al. Invest Ophthalmol Vis Sci 48:5690-5698, 2007) and ~ 1.7 % of LCA patients (Hanein et al. Hum Mutat 23:306-317, 2004).

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 <i>TULP1</i> gene:	\$ 640
CPT Codes:		
Sample Ascertainment x1	83890 \$ 30	DNA Isolation x1 83891 \$ 40
Amplification x 11	83898 \$ 180	Sequencing x 11 83904 \$ 270
Separation x1	83894 \$ 50	Interpretation/Report x1 83912 \$ 70

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

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