

X-linked Retinitis Pigmentosa (XLRP) via *RP2* Gene Sequencing – Test #680

Brief Description of Clinical Features: Retinitis Pigmentosa (RP; OMIM 268000) refers to a group of related eye disorders stemming from the degeneration of photoreceptor cells in the retina (for review, go to www.ncbi.nlm.nih.gov/books/NBK1417/). RP derives its name from retinal pigmentation changes. In RP patients, pigment granules accumulate in perivascular clusters, called bone-spicules, in the retinal pigment epithelium (RPE). The accumulation of pigment is typically accompanied by death of the photoreceptor cells, first rods and eventually cones. As a result, RP will often present first with night blindness and decreased peripheral vision due to systematic loss of rod cells, followed by deterioration of central vision acuity and day blindness from the loss of cone cells. RP has an incidence of ~1/3500 and can be inherited in autosomal recessive, autosomal dominant, X-linked, digenic and even mitochondrial patterns. Currently, mutations in over 30 genes are known to cause RP.

Genetics: X-linked RP (XLRP) is one of the most severe forms of RP, with early onset and rapid progression in males. Milder symptoms can also present in females, probably due to random X inactivation. At least five different genetic loci have been associated with XLRP: Xp11.2 (*RP2*), Xp21.1 (*RPGR*), Xp21.2-21.3 (*RP6*), Xp22 (*RP23*) and Xp26-27 (*RP24*) (<http://www.sph.uth.tmc.edu/RetNet/disease.htm>). To date, only the *RP2* and *RPGR* genes have been identified. *RPGR* encodes the retinitis pigmentosa GTPase regulator (Meindl et al. *Nat Genet* 13:35-42, 1996), and *RP2* encodes a protein of unknown function (Schwahn et al. *Nat Genet* 19:327-332, 1998). Mutations in *RPGR* account for the vast majority (~80%) of all XLRP cases while *RP2* accounts for about 10% of cases and the other loci likely account for the remainder (~10%) (Breuer et al. *Am J Hum Genet* 70:1545-1554, 2002; Sharon et al. *Am J Hum Genet* 73:1131-1146, 2003). The *RP2* gene consists of 5 exons with mutations found throughout all five exons; no founder mutations or mutational hotspots have been reported. Most mutations result in premature protein termination (i.e. frameshift, nonsense and splice-site), although a few missense mutations have also been identified (Mears et al. *Am J Hum Genet* 64:897-900, 1999; Hardcastle et al. *Am J Hum Genet* 64:1210-1215, 1999). Males hemizygous for mutations in *RP2* typically display classic features of RP, such as initial night blindness and loss of peripheral vision. Patients with mutations in *RP2* appear to retain less visual acuity than patients with mutations in *RPGR* (Sharon et al. 2003). Thus, knowledge of which XLRP gene is mutated is useful for making the most accurate long-term visual prognosis.

Description of This Particular Test: This test involves bidirectional DNA sequencing of all 5 coding exons of the *RP2* gene. As indicated, we will also sequence a single exon (Test #100; \$190) in family members of patients with a known mutation, or to confirm research results.

Reference Sequences: Genomic: NC_000023.10 mRNA: NM_006915.2 Protein: NP_008846.2 CCDS 14270.1

Indications for Test: Candidates for this test are patients with probable X-linked recessive Retinitis Pigmentosa (XLRP).

Sensitivity of Test: This test is predicted to detect a causative mutation in ~10-20% of all patients with presumptive XLRP (Breuer et al. 2002; Sharon et al. 2003).

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

Specimen Requirements: See page 4 of Requisition Form.

Price:	Sequencing of the <i>RP2</i> Gene:	\$ 540
CPT Codes:		
Sample Ascertainment x1	83890 \$ 30	DNA Isolation x1 83891 \$ 40
Amplification x7	83898 \$ 140	Sequencing x7 83904 \$ 210
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)

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