

**Retinitis Pigmentosa (Autosomal Dominant or Sporadic, Nonsyndromic)  
 via PRPF3 Gene Sequencing -- Test #669**

**Brief Description of Disorder:** Nonsyndromic Retinitis Pigmentosa (RP, OMIM # 268000) is a large group of inherited degenerative diseases of the retina characterized by abnormalities of the photoreceptors or the retinal pigment epithelium. It is a progressive disease. Symptoms usually begin with night blindness, progressing to constriction of the peripheral visual field and, eventually, to loss of central vision. The age of onset varies from childhood to middle age (Gu et al. J Med Genet 36:705-707, 1999). The clinical hallmarks are abnormal fundus with bone-spicule deposits and attenuated retinal vessels, abnormal electroretinographic findings and reduced visual fields (Daiger et al. Arch Ophthalmol 125:151-158, 2007). RP affects 1 in 3,000 people worldwide (Farrar et al. EMBO J 21:857-864, 2002). Genetic abnormalities are the primary cause of RP, which appears in diverse ethnic groups. See also the Foundation Fighting Blindness ([www.ffb.ca](http://www.ffb.ca)) and ([www.retina-international.org](http://www.retina-international.org)).

**Genetics:** RP is genetically and clinically heterogeneous. At least four distinct subgroups are recognized on the basis of the mode of inheritance and age of onset. These include autosomal dominant (AD-RP), autosomal recessive (AR-RP), X-linked, and digenic (Kajiwara et al. Science 264:1604-1608, 1994). In addition, RP can be inherited as a mitochondrial trait (Mansergh et al. Am J Hum Genet 64:971-985, 1999). About 50 % of patients with RP are isolated cases with no known affected relatives. It is unclear how many of these are real isolated cases caused by *de novo* mutations or inherited with low penetrance. Currently, mutations in 18 genes cause AD-RP or sporadic RP. These include the *PRPF3* gene. Three heterozygous mutations in the *PRPF3* gene have been identified in patients with RP, including sporadic and familial cases. These mutations are clustered in exon 11 and result in amino acid substitutions. Patients carrying *PRPF3* mutations have been reported to present with a mild phenotype and late onset (Chakarova et al. Hum Mol Genet 11:87-92, 2002; Gamundi et al. Hum Mut 29:869-878, 2008).

**Description of This Particular Test:** *PRPF3* encodes the Pre-mRNA-splicing factor 3 protein, which participates in the removal of introns from mRNA. *PRPF3* testing for RP at PreventionGenetics is performed in two tiers. In Tier 1, we sequence the coding region plus ~ 50 bp of flanking DNA on either side of exon 11. If Tier 1 is negative, we sequence the remaining 14 exons. We will sequence any single exon in family members of patients with known mutation or to confirm previous results.

**Reference Sequences:** Genomic: **NC\_000001.9** mRNA and Protein: **CCDS 951.1**

**Indications for Test:** The *PRPF3* gene is a candidate for RP patients with no mutations in the remaining RP genes.

**Sensitivity of Test:** Mutations in the *PRPF3* gene are detected in ~ 1 % of AD-RP patients (Daiger et al. Adv Exp Med Bio 613:203-209, 2008). PreventionGenetics plans to offer Tests for all genes known to cause RP and is committed to add new tests as the remaining RP genes are discovered.

**Turn Around Time:** Maximum of 40 calendar days.

**Specimen Requirements:** See page 4 of the Requisition Form.

**Prices:** Tier 1 alone \$ 190 Tier 2 alone \$ 890 Tiers 1 and 2 together \$ 890

| CPT Code | Description                  | Tier 1 only   | Tier 2 only   | Tier 1 and 2 together |
|----------|------------------------------|---------------|---------------|-----------------------|
| 83890    | Ascertainment                | \$ 30 (x 1)   | \$ 30 (x 1)   | \$ 30 (x 1)           |
| 83891    | DNA Isolation                | \$ 40 (x 1)   | \$ 40 (x 1)   | \$ 40 (x 1)           |
| 83898    | Amplification                | \$ 25 (x 1)   | \$ 255 (x 14) | \$ 260 (x 15)         |
| 83904    | Mutation Ident by Sequencing | \$ 35 (x 1)   | \$ 390 (x 14) | \$ 395 (x 15)         |
| 83894    | Separation                   | \$ 15 (x 1)   | \$ 80 (x 1)   | \$ 75 (x 1)           |
| 83912    | Interpretation and Report    | \$ 45 (x 1)   | \$ 95 (x 1)   | \$ 90 (x 1)           |
|          | <b>Totals</b>                | <b>\$ 190</b> | <b>\$ 890</b> | <b>\$ 890</b>         |

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

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