

**Retinitis Pigmentosa (Autosomal Dominant and Sporadic, Nonsyndromic)
 via *PRPF31* Gene Sequencing -- Test #666**

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. See also the Foundation Fighting Blindness (www.ffb.ca) and 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. RP affects all ethnic groups. Currently, mutations in 18 genes are known to cause AD-RP. These include the *PRPF31* gene. At least 40 heterozygous mutations in the *PRPF31* gene have been identified in patients with RP (Rio Frio et al. J Clin Invest 118:1519-1531, 2008), including familial and sporadic cases (Vithana et al. Mol Cell 8:375-381, 2001; Martínez-Gimeno et al. Invest Ophthalmol Vis Sci 44:2171-2177, 2003; Wang et al. Am J Med Genet 121A:235-239, 2003). The *PRPF31* mutations, most of which are novel, are distributed throughout the gene and are of various types. These mutations are associated with a wide clinical variability in terms of age of onset, disease severity and progression. *PRPF31* mutations have been detected in patients of various ethnic groups; however, the c.1142delG mutation has been found only in Japanese patients and accounts for the majority of Japanese RP (Taira et al. Jpn J Ophthalmol. 51:45-48, 2007).

Description of This Particular Test. *PRPF31* encodes the Pre-mRNA-processing factor 31 protein, which participates in the removal of introns from mRNA. Mutations in such proteins are expected to affect the splicing process of photoreceptor-specific genes resulting in abnormal gene products and ultimately retinal degeneration. This test involves bidirectional sequencing using genomic DNA of all 13 coding exons and splice sites of *PRPF31*. The full coding sequence of each exon plus ~ 50 bp of flanking-coding DNA on either side are sequenced. We will sequence any single exon in family members of patients with known mutation or to confirm previous results.

Reference Sequences: Genomic: **NC_000019.8** mRNA and protein: **CCDS 12879.1**

Indications for Test: The *PRPF31* gene is a candidate for RP patients with autosomal dominant or sporadic RP.

Sensitivity of Test: Mutations in the *PRPF31* gene account for ~ 8% of RP (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.

Price: **Sequencing of *PRPF31* Gene, Exons 2-14** **\$ 740**

CPT Codes:

Sample Ascertainment x1	83890 \$ 30	DNA Isolation x1	83891 \$ 40
Amplification x 13	83898 \$ 210	Sequencing x13	83904 \$ 310
Separation x1	83894 \$ 60	Interpretation/Report x1	83912 \$ 90

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, www.preventiongenetics.com