

## Retinitis Pigmentosa (Autosomal Dominant, Nonsyndromic) via *PRPH2* Gene Sequencing -- Test #663

**Brief Description of Clinical Features:** 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](http://www.ffb.ca)).

**Genetics:** Retinitis Pigmentosa is genetically and clinically heterogeneous (Koenekoop et al. Clin Exp Ophthalmol 35:473-485, 2007). At least four distinct subgroups are recognized on the basis of the mode of inheritance and age of onset. These include autosomal dominant-RP (AD-RP), autosomal recessive (AR-RP), X-linked, and digenic (Rivolta et al. Hum Mol Genet 11:1219-1227, 2002; 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). Genetic heterogeneity is documented within each subgroup. 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. AD-RP affects all ethnic groups, although mutations in particular genes have been identified in specific populations. Patients with AD-RP represent 15-25 % of all cases. Currently, mutations in eighteen (18) genes account for at least 58 % of AD-RP cases. These include the *PRPH2/RDS* gene. Over 32 different *PRPH2* causative mutations were found in patients with AD-RP. In addition, more than 53 mutations have been linked to a variety of human retinal diseases with related or overlapping phenotypes including Pattern Dystrophy, Macular Dystrophy, Cone-Rod Dystrophy and Retinitis Punctata Albescens. *PRPH2* mutations are distributed along the entire coding region of the gene and comprise missense and splice mutations, small deletions or insertions. The majority of *PRPH2* mutations are unique to single pedigrees.

**Description of This Particular Test:** The *PRPH2* gene encodes the peripherin/RDS protein, a structural transmembrane glycoprotein that contributes to the formation and stabilization of photoreceptors outer segments. This test involves bidirectional DNA sequencing of all 3 coding exons and splice sites of the *PRPH2* gene. The full coding sequence of each exon plus ~ 50 bp of flanking-coding DNA on either side is determined.

**Reference Sequences:** Genomic: **NC\_000006.10** mRNA and protein: **CCDS 4871.1**

**Indications for Test:** All patients with symptoms suggestive of AD-RP or sporadic RP. The *PRPH2* gene may also be a candidate for patients presenting with the following phenotypes: Pattern Dystrophy (OMIM #169150), Macular Dystrophy (OMIM #608161), Cone-Rod Dystrophy (OMIM #120970) and Retinitis Punctata Albescens (OMIM #136880). (See also [www.retina-international.org](http://www.retina-international.org)).

**Sensitivity of Test:** This test allows the detection of mutations in approximately 8.4 % of patients with AD-RP (Daiger et al. Adv Exp Med Bio 613:203-209, 2008). PreventionGenetics will offer Tests for all genes known to cause AD-RP, and is committed to add new tests as the remaining ADRP genes are discovered.

**Turn Around Time:** Maximum of 40 days, although many tests are completed in 3-4 weeks.

**Specimen Requirements:** See bottom of page 2 of Requisition Form.

**Price:** **Sequencing of *PRPH2* Gene, Exons 1-3** **\$ 420**

**CPT Codes:**

|                         |       |        |                          |       |        |
|-------------------------|-------|--------|--------------------------|-------|--------|
| Sample Ascertainment x1 | 83890 | \$ 30  | DNA Isolation x1         | 83891 | \$ 40  |
| Amplification x4        | 83898 | \$ 110 | Sequencing x4            | 83904 | \$ 150 |
| Separation x1           | 83894 | \$ 30  | Interpretation/Report x1 | 83912 | \$ 60  |

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