

**Retinitis Pigmentosa (Autosomal Dominant, Nonsyndromic)  
 via *RHO* Gene Sequencing -- Test #661**

**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; Kajiwarara 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); and 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 (Fishman, Arch Ophthalmol 96:822-826, 1978). Currently, mutations in eighteen (18) genes account for at least 58 % of AD-RP cases. Mutations in the *RHO* gene represent the most common cause of AD-RP. Over 128 different *RHO* causative mutations were reported. *RHO* mutations are distributed along the entire coding region of the gene. Although most mutations are missense resulting in amino acid substitutions, splice mutations and small deletions and insertions were also reported. Rare *RHO* mutations were found in patients with AR-RP (OMIM # 268000) autosomal dominant congenital stationary night blindness (CSNB, OMIM # 610445), and Retinitis punctata albescens (OMIM # 136880). (See also [www.retina-international.org](http://www.retina-international.org)).

**Description of This Particular Test:** The *RHO* gene encodes the rhodopsin protein, a retinal protein responsible for the formation of photoreceptors. This test involves bidirectional DNA sequencing of all 5 coding exons and splice sites of the *RHO* gene. The full coding sequence of each exon plus ~ 50 bp of flanking-coding DNA on either side are sequenced.

**Reference Sequences:** Genomic: **NC\_000003.10** mRNA and protein: **CCDS 3063.1**

**Indications for Test:** All patients with symptoms suggestive of AD-RP or sporadic RP. The *RHO* gene may also be candidate for patients with AR-RP, patients with CSNB, and patients with Retinitis punctata albescens with no mutations detected in the genes known to cause these three diseases.

**Sensitivity of Test:** This test allows the detection of mutations in approximately 28 % of patients with AD-RP. PreventionGenetics will offer Tests for all genes known to cause AD-RP, and is committed to add new tests as the remaining AD-RP genes are discovered.

**Turn Around Time:** Maximum of 40 days, although many tests are completed in 2-3 weeks.

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

**Price:                      Sequencing of *RHO* Gene, Exons 1-5    \$ 540**

**CPT Codes:**

Sample Ascertainment	83890	\$ 30	DNA Isolation	83891	\$ 40
Amplification x6	83898	\$ 130	Sequencing x6	83904	\$ 210
Separation	83894	\$ 50	Interpretation/Report	83912	\$ 80

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

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