

## Achromatopsia via *PDE6C* Gene Sequencing -- Test #694

**Brief Description of Clinical Features:** Achromatopsia (ACHM) is a congenital cone rod dystrophy (CRD) that can be distinguished from other CRDs on the basis of primary cone involvement, stationary course, and normal fundus (Hamel Orphanet J Rare Dis 2:7, 2007). Two clinical types of achromatopsia, complete and incomplete, are recognized. In patients with complete achromatopsia, symptoms usually begin in infancy and include nystagmus, low visual acuity, photophobia, severe color vision defects, and selective absence of functioning cone photoreceptor cells in electroretinogram (ERG) findings. Patients with incomplete achromatopsia retain residual functioning cone cells. In addition, they have mild visual acuity and mild color vision defects. The prevalence of complete achromatopsia is 1 per 30,000 people worldwide (Michaelides et al. Br. J. Ophthalmol 88, 291–297, 2004). However, in the Micronesian atoll of Pingelap, achromatopsia affects ~ 5 % of the island population (Morton et al. Am J Hum Genet 24:277-289, 1972).

**Genetics:** Achromatopsia is a heterogeneous genetic disease that is inherited in an autosomal recessive manner. It is caused by defects in various genes that encode important elements of the cone phototransduction process. Mutations in four genes, including *PDE6C* (Chang et al. Proc Natl Acad Sci U S A 106:19581-19586, 2009; Thiadens et al. Am J Hum Genet 85:240-247, 2009) have been identified in patients with achromatopsia. To date, ~15 different *PDE6C* causative mutations have been reported. Mutations include missense, nonsense, splicing, and small insertions and/or deletions. No large deletions, duplications, or complex rearrangements have been reported. In addition to achromatopsia, *PDE6C* mutations were identified in patients with autosomal recessive, early onset progressive cone dystrophy (arCD); suggesting that ACHM and arCD are clinically and genetically overlapping disorders (Thiadens et al. 2009).

**Description of This Particular Test:** The *PDE6C* gene encodes the alpha subunit of phosphodiesterase in cone photoreceptor cells. This test involves bidirectional DNA sequencing of all 21 coding exons and splice sites of the *PDE6C* gene. The full coding sequence of each exon plus ~ 50 bp of flanking DNA on either side are sequenced. As indicated, we will sequence any single (Test #100) or double (Test #200) exons in family members of patients with known mutations or to confirm previous results.

**Reference Sequences:** Genomic: NC\_000010.10 mRNA: NM\_006204.3 Protein: NP\_006195.3 (CCDS 7429.1)

**Indications for Test:** Patients with normal rod response and absence of cone response in ERG findings, and no mutations in the *CNGB3*, *CNGA3* and *GNAT2* genes (Kohl et al. GeneReviews, 2010, [www.genetests.org](http://www.genetests.org)).

**Sensitivity of Test:** About 2% of achromatopsia patients with known causative mutations have mutations in *PDE6C* (Thiadens et al. 2009).

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

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

<b>Price:</b>	<b>Sequencing of <i>PDE6C</i> Gene</b>	<b>Exons 1-22</b>	<b>\$ 1090</b>
<b>CPT Codes:</b>			
Sample Ascertainment x1	83890	\$ 30	DNA Isolation x1 83891 \$ 40
Amplification x 21	83898	\$ 330	Sequencing x 21 83904 \$ 500
Separation x1	83894	\$ 80	Interpretation/Report x1 83912 \$ 110

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

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