

Achromatopsia via *CNGB3* Gene Sequencing -- Test #692

Brief Description of Clinical Features: Achromatopsia 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 *CNGB3* (Sundin et al. Nat Genet 25:289-293, 2000), have been identified in patients with achromatopsia. At least 37 different *CNGB3* causative mutations have been reported. Most mutations are expected to result in truncated proteins and include nonsense and splice site mutations, and small insertions and/or deletions. Only three missense mutations were reported to date. No large deletions, duplications, or complex rearrangements have been reported. A founder missense mutation, c.1304C>T, causes achromatopsia in the Pingelap population (Sundin, 2000). In addition to achromatopsia (OMIM 262300), *CNGB3* mutations were identified in patients with juvenile onset macular degeneration (OMIM 248200; Nishiguchi et al. Hum Mutat 25:248-258, 2005) and patients with progressive cone dystrophy (Michaelides et al. Invest Ophthalmol Vis Sci 45:1975-1982, 2004).

Description of This Particular Test: The *CNGB3* gene encodes the beta subunit of the cyclic nucleotide-gated cation channel in cone photoreceptor cells. This test involves bidirectional DNA sequencing of all 18 exons and splice sites of the *CNGB3* 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_000008.10 mRNA: NM_019098.4 Protein: NP_061971.3 (CCDS 6244.1)

Indications for Test: Patients with normal rod function and absence of cone response in ERG findings (Kohl et al. GeneReviews, 2009, www.genetests.org).

Sensitivity of Test: This test will detect mutations in up to 50 % of patients with clinical diagnosis of achromatopsia (Kohl et al. Eur J Hum Genet 13:302-308, 2005).

Turnaround 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 *CNGB3* Gene, Exons 1 - 18 \$ 980

CPT Codes:

Sample Ascertainment x1	83890 \$ 30	DNA Isolation x1	83891 \$ 40
Amplification x 18	83898 \$ 290	Sequencing x18	83904 \$ 440
Separation x1	83894 \$ 70	Interpretation/Report x1	83912 \$ 110

Accreditation: CLIA ID #: 52D1027685 (expires 1/18/13) (CAP#: 7185561, AU ID: 1407125 expires 12/20/11)

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