

Achromatopsia via GNAT2 Gene Sequencing -- Test #693

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 *GNAT2* (Kohl et al. Am J Hum Genet 71:422–425, 2002), have been identified to date in patients with achromatopsia. About 10 different *GNAT2* causative mutations have been reported. All mutations result in premature protein termination.

Description of This Particular Test: The *GNAT2* gene encodes the alpha subunit of transducin, a G-protein that is specifically expressed in the cone photoreceptor cells. This test involves bidirectional DNA sequencing of all 8 exons and splice sites of the *GNAT2* 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_000001.10 mRNA: NM_005272.3 Protein: NP_005263.1 (CCDS 803.1)

Indications for Test: Patients with normal rod function and absence of cone response in ERG findings, and no mutations in the *CNGB3* or *CNGA3* genes (Kohl et al. GeneReviews, 2009, www.genetests.org).

Sensitivity of Test: This test will detect mutations in ~ 2% of patients with clinical diagnosis of achromatopsia (Kohl et al. 2002).

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 *GNAT2* Gene, Exons 1 - 8 \$ 570

CPT Codes:

Sample Ascertainment x1	83890 \$ 30	DNA Isolation x1	83891 \$ 40
Amplification x8	83898 \$ 150	Sequencing x8	83904 \$ 220
Separation x1	83894 \$ 40	Interpretation/Report x1	83912 \$ 90

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

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