Achromatopsia, Cone, and Cone-rod Dystrophy: Deletion/Duplication Panel

**Test Code:** MD131
**Turnaround time:** 2 weeks
**CPT Codes:** 81228 x1, 81479 x1

**Condition Description**

Complete achromatopsia, or rod monochromatism, is an autosomal recessive disease affecting cone function that is characterized by intense photophobia, deficient cone-mediated electroretinogram, reduced visual acuity, a normal or near normal fundus appearance, pendular nystagmus, and impaired color discrimination for all cone classes. Temporal optic atrophy, a slight macular retinal pigment epithelial disturbance, may also be seen on fundus exam. Pathogenic variants in five different genes have been identified as causing achromatopsia (CNGB3, CNGA3, GNAT2, PDE6C, and PDE6H). Thus far, most pathogenic variants have been identified in the CNGB3 and CNGA3 genes.

Cone dystrophies are diagnosed by an abnormal or nonrecordable photopic ERG and a normal scotopic ERG, while peripheral visual fields remain normal. All three inheritance patterns, autosomal dominant, autosomal recessive, and X-linked, have been found in the cone degenerations. Symptoms of cone dysfunction include loss of visual acuity, photophobia (light intolerance), and progressive color vision loss. Retinal pigment epithelial loss and pigment deposition may be seen in later stages. Mild to severe temporal optic atrophy, bull’s eye maculopathy with or without tapetal reflexes or macular atrophy may be seen.

Cone-rod dystrophy (CORD) is characterized by an initial loss of color vision and visual acuity, followed by nystagmus (night blindness) and loss of peripheral visual fields. In extreme cases, these progressive symptoms are accompanied by widespread, advancing retinal pigmentaition and chorioretinal atrophy of the central and peripheral retina.

These conditions can have overlapping clinical presentations.

Please note, the RAB28 gene is not included on the NGS panel at this time due to the presence of at least 2 pseudogenes. For clinicians that would like RAB28 analysis if all other genes test negative, we request consultation with EGL directly.

**References:**
- OMIM
- GeneReviews

**Genes**

ABCA4, ADAM9, AIPL1, BEST1, C8orf37, C4BP4, CACNA1F, CACNA2D4, CDHR1, CEP290, CERKL, CNGA3, CNGB3, CNNM4, CRX, GNAT2, GUCA1A, GUCA1B, GUCA2D, KCNV2, PAX6, PDE6C, PDE6H, PITPNM3, PROM1, PRPH2, RAX2, RBP4, RDH5, RGS9, RGS9BP, RIMS1, RPGR, RPGRIP1, SEMA4A, UNC119

**Indications**

This test is indicated for:

- Confirmation of a clinical diagnosis of achromatopsia, cone, and cone-rod dystrophy.
- Carrier testing in adults with a family history of achromatopsia, cone, and cone-rod dystrophy.

**Methodology**

**Deletion/Duplication Analysis:** DNA isolated from peripheral blood is hybridized to a gene-targeted CGH array to detect deletions and duplications. The targeted CGH array has overlapping probes that cover the entire genomic region. Please note that a “backbone” of probes across the entire genome are included on the array for analytical and quality control purposes. Rarely, off-target copy number variants causative of disease may be identified that may or may not be related to the patient's phenotype. Only known pathogenic off-target copy number variants will be reported. Off-target copy number variants of unknown clinical significance will not be reported.

**Detection**

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**Deletion/Duplication:** Detection is limited to duplications and deletions. The CGH array will not detect point or intronic pathogenic variants. Results of molecular analysis must be interpreted in the context of the patient's clinical and/or biochemical phenotype.

**Specimen Requirements**

Submit only 1 of the following specimen types

**Type: Whole Blood**

Specimen Requirements:

In EDTA (purple top) tube:
- Infants (2 years): 3-5 ml
- Older Children & Adults: 5-10 ml

Specimen Collection and Shipping: Ship sample at room temperature with overnight delivery.

**Type: Isolated DNA**

Specimen Requirements:

In microtainer: 10 ug

Isolation using the Qiagen™ Puregene kit for DNA extraction is recommended.

Specimen Collection and Shipping: Refrigerate until time of shipment in 100 ng/ul of TE buffer. Ship sample at room temperature with overnight delivery.

**Special Instructions**

Please include fundus photographs, electroretinogram (ERG) findings, visual field findings, and visual acuity, if available, for expert review and clinical correlation with test results.

**Related Tests**

- Eye Disorders: Comprehensive Sequencing and Deletion/Duplication Panels.
- Achromatopsia, Cone, and Cone-rod Dystrophy: Sequencing Panel.