

Achromatopsia Panel

Achromatopsia also known as: Pingelapese blindness, total color blindness with myopia, achromatopsia with myopia, ACHM1, rod monochromatism 1, rod monochromic, RMCH1.

Panel Gene List: CNGA3 and CNGB3

Clinical Features:

Achromatopsia is a rare congenital autosomal recessive disorder. This disorder is characterized by an inability to discriminate colors, a low visual acuity, pendular nystagmus, and photodysphoria (extreme photophobia) under daylight conditions. Examination of these patients by ophthalmoscope reveals a mild foveal hypoplasia, while ERG recordings and psychophysical tests reveal absent photopic responses and intact scotopic responses^{1,2,4,5,7}. Variants in the CNGA3, CNGB3, GNAT2, PDE6C, ATF6 and PDE6H genes, have been shown to cause achromatopsia^{3,4,6}.

Inheritance Pattern/Genetics:

Autosomal recessive

Test Methods:

The coding regions and splice junctions of the 2 genes of this panel are enriched using a proprietary targeted capture system developed by GeneDx. The targeted regions are sequenced simultaneously by massively parallel (NextGen) sequencing on an Illumina platform with paired-end reads. Bi-directional sequence is assembled, aligned to reference gene sequences based on human genome build GRCh37/UCSC hg19, and analyzed for sequence variants. Capillary sequence is used to confirm all potentially pathogenic variants and to obtain sequence for regions where fewer than 19 reads are achieved by NextGen sequencing.

Test Sensitivity:

CNGA3 gene: Cyclic nucleotide gated channel alpha 3

Variants in the CNGA3 gene have been reported in approximately 20% of the patients with complete or incomplete achromatopsia^{8,9}.

CNGB3 gene: Cyclic nucleotide gated channel beta 3

Variants in the CNGB3 gene have been reported in approximately 50% of the patients diagnosed with autosomal recessive achromatopsia^{2,9}, with the c.1148delC variant accounting for over 70-75% of all CNGB3 mutant alleles^{2,9}. Kohl et al., reported that approximately 91% of variant positive individuals were either homozygous or compound heterozygous for the variants identified, while only approximately 9% were heterozygous for a single variant.

Gene	Protein	Inheritance	Disease Associations
<i>CNGA3</i>	Cyclic nucleotide gated channel alpha 3	AR	Achromatopsia-2
<i>CNGB3</i>	Cyclic nucleotide gated channel beta 3	AR	Achromatopsia-3; macular degeneration, juvenile

References:

1. Kohl et al., (2000) Hum Mol Genet 9:2107-2116 (PMID: 10958649)
2. Kohl et al., (2005) Eur J Hum Genet 13:302-308 (PMID:15657609)
3. Kohl et al., (2012) Am J Hum Genet 91:527-532 (PMID: 22901948)
4. Kohl et al., (2015) Nature Genet 47:757-765 (PMID: 26029869)
5. Sundin et al., (2000) Nat Genet 25:289-293 (PMID: 10888875)
6. Thiadens et al., (2009) Am J Hum Genet 85:240-247 (PMID: 19615668)
7. Thiadens et al., (2010) Ophthalmology 117:825-830 (PMID: 20079539)
8. Wissinger et al., (2001) Am J Hum Genet 69:722-37 (PMID: 11536077)
9. Wiszniewski et al., (2007) Hum Genet 121:433-439 (PMID: 17265047)