

RDH5 Gene Testing in Fundus Albipunctatus

Clinical Features:

Fundus albipunctatus is a retinal disorder characterized by night blindness and delayed dark adaptation after exposure to bright light, which typically presents during early childhood. The fundi of affected individuals contain multiple small, white or pale yellow dots in the retinal pigment epithelium, which may or may not involve the macula. These dots can remain unchanged, become more prominent, or can fade during aging; new dots may also appear. The dark-adaptation curve of affected individuals features prolonged recovery of cone and rod sensitivity and electroretinogram cone and rod amplitudes are markedly reduced after 30-40 minutes of dark adaptation; however, they may come to normal or near-normal levels after many hours of adaptation.¹ Niwa et al. showed that approximately 38% of individuals with FA have extensive cone dysfunction.² Variants in the *RLBP1* gene have also been reported in FA patient. Genetic testing for *RLBP1* is available at GeneDx; please refer to its gene-specific information sheet for further information.

Inheritance Pattern/Genetics:

Pathogenic variants in the *RDH5* are inherited in an autosomal recessive manner. The vast majority of pathogenic variants observed in the *RDH5* gene are missense substitutions; however, frameshift variants have also been observed.^{3,5,6}

Test Sensitivity:

The majority of studies performed examining fundus albipunctatus have been case studies or small familial studies. The identification of *RDH5* variants in affected individuals with FA in these studies has ranged from 75% to 100%.^{7,3,4}

Test Methods:

Using genomic DNA from the submitted specimen, the coding regions and splice junctions of the requested gene are PCR amplified and capillary sequencing is performed. Bi-directional sequence was assembled, aligned to reference gene sequences based on NCBI RefSeq transcript and human genome build GRCh37/UCSC hg19, and analyzed for sequence variants. Concurrent deletion/duplication testing is performed for most, if not all, of the coding exons using exon-level oligo array CGH (ExonArrayDx), and data analysis is performed using gene-specific filtering. Probe sequences and locations are based on human genome build GRCh37/UCSC hg19. Reported clinically significant variants are confirmed by an appropriate method. Sequence and copy number variants are reported according to the Human Genome Variation Society (HGVS) or International System for Human Cytogenetic Nomenclature (ISCN) guidelines, respectively. Reportable variants include pathogenic variants, likely

pathogenic variants and variants of uncertain significance. Likely benign and benign variants, if present, are not routinely reported but are available upon request.

References:

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2. Niwa et al., (2005) Invest Ophthalmol Vis Sci 46(4):1480-5.
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4. Nakamura et al. (2003) Doc Ophthalmol 107(1):3-11.
5. Liden et al., (2001) J Biol Chem 276(52):49251-7.
6. Driessen et al., (2001) Ophthalmology 108(8):1479-84.
7. Yamamoto H et al., (1999) Nat Genet 22:188-91.