

CERKL Gene Analysis in Autosomal Recessive Retinitis Pigmentosa (arRP)

Clinical Features:

Retinitis Pigmentosa (RP) is a group of disorders involving progressive degeneration of the retina that leads to severe visual impairment. The age of onset of visual symptoms is variable from early childhood to adulthood and is usually more severe if the disorder is inherited as an autosomal trait. The disorder usually manifests with decline and loss of night vision during adolescence, followed by loss of peripheral vision in young adulthood, and loss of central vision in later life due to the progressive loss of rod and cone photoreceptors. Common symptoms include night blindness and a decreasing visual field, leading to tunnel vision, legal blindness or, in many cases, complete blindness. Clinical hallmarks are an abnormal fundus with bone-spicule deposits and attenuated retinal vessels. The electroretinogram (ERG) findings in RP patients show reduced rod and cone response amplitudes, which is moderate in dominant inheritance and barely detectable in recessive and X-linked patients.

Inheritance Pattern:

Autosomal recessive

Test Sensitivity:

Pathogenic variants in the CERKL gene have been identified in several extended families of various ethnicities who were diagnosed with autosomal recessive retinitis pigmentosa (arRP).¹⁻⁶ Pathogenic variants in this gene have also been reported in approximately 2% of autosomal recessive cone-rod dystrophy in patients who tested negative for ABCA4 variants.⁷

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 is 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 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:

1. Tuson et al. (2004) *Am. J. Hum. Genet.* 74 (1):128-38 (PMID: 14681825)
2. Auslender et al. (2007) *Invest. Ophthalmol. Vis. Sci.* 48 (12):5431-8 (PMID: 18055789)
3. Ali et al. (2008) *Mol. Vis.* 14 :1960-4 (PMID: 18978954)
4. Avila-Fernandez et al. (2008) *Invest. Ophthalmol. Vis. Sci.* 49 (6):2709-13 (PMID: 18515597)
5. Aleman et al. (2009) *Invest. Ophthalmol. Vis. Sci.* 50 (12):5944-54 (PMID: 19578027)
6. Tang et al. (2009) *Arch. Ophthalmol.* 127 (8):1077-8 (PMID: 19667359)
7. Littink et al. (2010) *Invest. Ophthalmol. Vis. Sci.* 51 (11):5943-51 (PMID: 20554613)