

RP2 Gene analysis in X-linked Retinitis Pigmentosa

Clinical Features:

X-linked Retinitis Pigmentosa (XLRP) affects 10-20% of families with retinitis pigmentosa. This particular form of RP is rather severe in that affected males show first symptoms, such as night blindness and lack of dark adaptation, already within the first decade of life. In the second decade, patients usually have a reduced visual field and visual acuity, followed by complete blindness by the third or fourth decade of life. Female carriers may also be affected with a milder form of disease with peripheral pigmentary changes in the retina.

Genetics:

X-linked, heterozygous females may express a mild phenotype. Retinitis pigmentosa (RP), including its non-syndromic and syndromic forms, has a worldwide prevalence of 1/3000-1/7000. Non-syndromic RP encompasses 65% of all cases, or about 650,000 people in the United States. RP is genetically heterogeneous and over 35 genes have been implicated in its pathogenesis. Approximately 30% of cases are autosomal dominant inherited, 20% are autosomal recessive, 15% are X linked, and 5% represent early-onset forms of autosomal recessive Leber congenital amaurosis. Only two genes, *RP2* and *RPGR* are known to cause X-linked RP.

Test Sensitivity:

Variants in the *RP2* gene are found in about 8-15% of patients with X-linked RP, while variants in the *RPGR* gene have been reported in 70-80% of XLRP patients. Deletions of one or more exons of the *RP2* gene have been reported previously in affected males. Gene copy number analysis by ExonArrayDx enables detection of both complete and partial *RP2* gene deletions in female carriers.

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 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:

1. Dandekar et al (2004) Br J Ophthalmol 88:528-532.
2. Prokisch et al., (2007) Investigative Ophthalmology & Visual Science 48:4012-4018.
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5. Jin et al., (2006) Molecular Vision 12:1167-1174.