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 Methods:
Variant analysis of the RP2 gene is performed on genomic DNA from the submitted specimen using bi-directional sequence analysis of exons 1-5 and corresponding intron/exon boundaries. In females, where sequencing cannot detect large deletions, targeted array CGH analysis with exon-level resolution (ExonArrayDx) is available to evaluate for a deletion or duplication of one or more exons of this gene. Variants found in the first person of a family to be tested are confirmed by repeat analysis using sequencing, restriction fragment analysis, or another appropriate method.

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.

References:

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