RS1 Gene Analysis in X-Linked Juvenile Retinoschisis

Clinical Features:
X-linked retinoschisis is the most common cause of juvenile retinal degeneration in males usually presenting between age 5 and 10 years, and resulting in decreased visual acuity during childhood and adolescence. Vision after that period generally stabilizes at 20/60-20/120, although progressive visual deterioration often occurs later in life. The disorder is characterized by splitting of the nerve fiber layer in the retina. Eye findings include macular schisis, often in a spoke-like pattern; peripheral (usually inferotemporal) schisis in about 50% of subjects; “vitreous veils”; and a decreased b-wave with an intact a-wave on electroretinogram (ERG). The prevalence is estimated to be between 1/5,000 and 1/25,000 males. Although distinct from retinal detachment, retinoschisis may eventually lead to detachment of the retina or retinal atrophy resulting in blindness.

Inheritance Pattern/Genetics:
X-linked recessive

Test Methods:
Using genomic DNA obtained from the submitted biological material, bi-directional sequence of the coding region and splice junctions of the six exons of the RS1 gene is analyzed to evaluate for a variant in this gene. 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:
Several studies have shown the sensitivity of full gene sequencing in affected males to be 90-95%. Due to the limitations of sequence analysis, the sensitivity of our testing is slightly reduced in female index cases as deletions spanning one or more exons, which have been shown to occur in approximately 5% of cases, may not be detected in females.

Variants include missense, nonsense and splice site alterations. Small deletions and insertions have also been observed, as have intragenic rearrangements and deletions spanning one or more exons. Variants are found throughout the gene, with some clustering of variant in the 5’ end of the coding sequence.

References:
1. The Retinoschisis Consortium, Functional implications of the spectrum of mutations found in 234 cases with X-linked juvenile retinoschisis, Human Molecular Genetics 7:1185-1192 (1998)

2. Hiriyanna, K.T. et al., Novel mutations in XLRS1 causing retinoschisis, including first evidence of putative leader sequence change, Human Mutation 14:423-427 (1999)
3. Sieving PA et al., Juvenile Retinoschisis: A Model For Molecular Diagnostic Testing of X-Linked Ophthalmic Disease, Am Ophth Soc Vol XCV11 (1999)