NR2E3 Gene Analysis in Enhanced S-Cone Syndrome / Goldmann-Favre Syndrome / Autosomal Dominant Retinitis Pigmentosa

Disorder also known as: Goldmann-Favre syndrome; retinoschisis with early hemeralopia; Favre hyaloideoretinal degeneration; Retinitis Pigmentosa 37

Clinical Features:
Enhanced S-Cone syndrome (ESCS): is an autosomal recessive retinopathy, that results in a gain-of-function and excess numbers of S-cone photoreceptors, which makes these patients hypersensitive to blue light. These patients also experience a near absence of function of the majority rod receptor. Patients with ESCS suffer night blindness early in life and experience varying degrees of deficiency in long and middle cone receptor vision. Visual acuity is variable from normal to severely reduced. Varying degrees of retinal degeneration is also apparent upon examination.

Goldmann-Favre syndrome: is possibly a different expression of NR2E3-related disease and is associated with more severe degree of clinically evident retinal degeneration than is typically seen with ESCS. Patients with Goldmann-Favre syndrome typically experience retinoschisis or edema of the macula, pigmentary degeneration of the retina, hemeralopia, liquefied vitreous body with pre-retinal structures, and extinguished electroretinogram. Cataract is also a common feature.

Retinitis Pigmentosa: Patients with this particular form of autosomal dominant retinitis pigmentosa (adRP) were reported to have 3 concentric rings of hyperautoflourescence around the fovea, along the vascular arcades, and in the far periphery.

Genetics:
ESCS and Goldmann-Favre syndrome: Autsosomal recessive with variable expressivity
Retinitis Pigmentosa: Autosomal dominant

Test Methods:
Using genomic DNA obtained from the submitted biological material, bi-directional sequencing of all eight coding exons of the NR2E3 gene is performed. If sequencing identifies a variant on only one allele of the NR2E3 gene, and if clinically indicated, reflex deletion/duplication testing (ExonArrayDx) will be performed at no additional charge to evaluate for a deletion/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:

Pathogenic variants in the NR2E3 gene have been reported in approximately 75-96% of patients diagnosed with ESCS or Goldmann-Favre syndrome.[1,2,5] Approximately 8% of these patients will only have 1 identifiable variant in the NR2E3 gene.[1,5] In one study, a variant in the NR2E3 gene was identified in a family diagnosed with autosomal dominant retinitis pigmentosa (adRP), and in a further 2 out of 46 (~4%) probands diagnosed with RP.[3]

References:

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2. Bandah et al., (2009) Arch Ophthalmol 127(3):297-301
3. Coppieters et al., (2007) Am J Hum Genet 81:147-157
4. Solnas et al., (2008) Clin Genet 73:360-366
5. Wright et al., (2004) Hum Mutat #756 Online.