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 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]

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. If present, apparently homozygous sequence variants are confirmed using alternate primer pairs to significantly reduce the possibility of allele drop-out. 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. Audo et al., (2008) Invest Ophthalmol Vis Sci 49:2082-2093
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.