RHO Gene Analysis in Autosomal Dominant Retinitis Pigmentosa (adRP)

Clinical Features:
Retinitis Pigmentosa (RP) is a group of disorders involving progressive degeneration of the retina that leads to severe visual impairment. The age of onset of visuals symptoms is variable from early childhood to adulthood and is usually more severe if the disorder is inherited as an autosomal trait. The disorder usually manifests with decline and loss of night vision during adolescence, followed by loss of peripheral vision in young adulthood, and loss of central vision in later life due to the progressive loss of rod and cone photoreceptors. Common symptoms include night blindness and a decreasing visual field, leading to tunnel vision, legal blindness or, in many cases, complete blindness. Clinical hallmarks are an abnormal fundus with bone-spicule deposits and attenuated retinal vessels. The electroretinogram (ERG) findings in RP patients show reduced rod and cone response amplitudes, which is moderate in dominant inheritance and barely detectable in recessive and X-linked patients.

Inheritance Pattern/Genetics:
Autosomal dominant

Test Sensitivity:
Rhodopsin variants are the most common cause of adRP, and are found in approximately 26-28% of patients (Daiger et al., 2008). RHO variants can also cause autosomal recessive RP (arRP), congenital stationary night blindness (CSNB) and retinitis punctate albescens (RPA).

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. Daiger et al. (2008) Adv Exp Med Biol. 613:203-9 (PMID: 18188946)