CHM Gene Analysis in Choroideremia

Disorder also known as: Progressive Tapetochoroidal dystrophy

Clinical Features:
Choroideremia (CHM) is an X-linked progressive degeneration of the photoreceptors, retinal pigment epithelium, and choriocapillaris. Affected males experience night blindness, followed by progressive loss of peripheral vision that becomes more evident by the second and third decade of life leading to tunnel vision and often blindness. The early findings in a male with choroideremia are very similar to those of carrier females. Disruption of the retinal pigment epithelia starts in the mid-periphery. The progressive loss of the choriocapillaris results in the exposure of the choroidal vessels. Female carriers can be identified clinically by the presence of patchy areas of atrophy of the retinal pigment epithelium but show no serious visual impairment.

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 fifteen exons of the CHM gene is analyzed to evaluate for a variant in this gene. 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 found CHM variants in 74-95% of affected males. Due to technical limitations, the sensitivity of DNA sequencing is slightly reduced in female carriers, as deletions spanning one or more exons, which have been shown to occur in approximately 4-20% of cases, may not be detectable. However, such heterozygous partial or whole gene deletions may be detected by subsequent targeted array CGH analysis.

References:

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