

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 Sensitivity:

Several studies have found CHM variants in 74-95% of affected males. Deletions spanning one or more exons, which have been shown to occur in approximately 4-20% of cases would be detected in females via the ExonArrayDx portion of this test.

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. Cremers et al., (1990) Nature 347:674-7 (PMID: 2215697)
2. McTaggart et al., (2002) Hum Mutat Sep;20(3):189-96 (PMID: 12203991)
3. Genetic Diseases of the Eye. Ed. Elias I. Traboulsi. New York and Oxford: Oxford University Press, 1998.
4. Smaoui et al., (2007) Mutation Spectrum of the CHM Gene in Patients With Choroideremia. ARVO May 6-10, 2007 Fort Lauderdale, Florida.
5. <http://www.retina-international.org/sci-news/repmut.htm>
6. Esposito et al., (2011) Hum Mut 32(12):1460-9 (PMID: 21905166)
7. Li et al., (2014) Int J Molec Med 34(2):573-7 (PMID: 249