Choroideremia: *CHM* Gene Sequencing

**Test Code:** SCHMX  
**Turnaround time:** 4 weeks  
**CPT Codes:** 81479 x1

### Condition Description

Choroideremia is an X-linked disorder causing chorioretinal degeneration with an incidence of 1 in 50,000. Mutations in the *CHM* (Xq21.2) gene cause this condition.

The characteristic feature of choroideremia is the progressive chorioretinal degeneration in affected males. In males, the symptoms range from night blindness to peripheral visual field loss with central vision preserved until late in life. About 30% of males have posterior subcapsular cataracts. Carrier females are usually asymptomatic but the chorioretinal degeneration can be picked up by fundus examination. They also exhibit mild symptoms after the second decade of life. In cases of skewed X-inactivation, females can develop symptoms similar to affected males.

Both sequencing and deletion/duplication mutations have been described in the *CHM* gene. A founder splice site mutation in exon 13 is common in the Finnish population. Rarely, *CHM* can be part of a more severe contiguous gene deletion syndrome involving Xq21.

For patients with suspected choroideremia, sequence analysis is recommended as the first step in mutation identification. For individuals in whom mutations are not identified by full gene sequencing, deletion/duplication analysis is appropriate.

### References:

- *GeneReviews*
- MacDonald et al. (2009), *Surv Ophthalmol*, 54:401–7
- OMIM #303100: Choroideremia
- OMIM #300390: *CHM* gene

### Genes

**CHM**

### Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of choroideremia.
- Carrier testing in adults with a family history of choroideremia.

### Methodology

PCR amplification of 15 exons contained in the *CHM* gene is performed on the patient's genomic DNA. Direct sequencing of amplification products is performed in both forward and reverse directions, using automated fluorescence dideoxy sequencing methods. The patient's gene sequences are then compared to a normal reference sequence. Sequence variations are classified as mutations, benign variants unrelated to disease, or variations of unknown clinical significance. Variants of unknown clinical significance may require further studies of the patient and/or family members. This assay does not interrogate the promoter region, deep intronic regions, or other regulatory elements, and does not detect large deletions.

### Detection

**Clinical Sensitivity:** Sequencing and whole/partial gene deletions account for approximately 60-95% of cases. Mutations in the promoter region, some mutations in the introns and other regulatory element mutations cannot be detected by this analysis. Large deletions will not be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's clinical and/or biochemical phenotype.

**Analytical Sensitivity:** ~99%

### Specimen Requirements

**Submit only 1 of the following specimen types**

**Type:** Saliva

**Specimen Requirements:**

- Oragene™ Saliva Collection Kit
- Orangene™ Saliva Collection Kit used according to manufacturer instructions. Please contact EGL for a Saliva Collection Kit for patients that cannot provide a blood sample.

**Specimen Collection and Shipping:**

Please do not refrigerate or freeze saliva sample. Please store and ship at room temperature.
Type: DNA, Isolated

Specimen Requirements:
- Microtainer
- 8µg
- Isolation using the Perkin Elmer™Chemagen™ Automated Extraction method or Qiagen™ Puregene kit for DNA extraction is recommended.

Specimen Collection and Shipping:
- Refrigerate until time of shipment in 100 ng/µL in TE buffer. Ship sample at room temperature with overnight delivery.

Type: Whole Blood (EDTA)

Specimen Requirements:
- EDTA (Purple Top)
  - Infants and Young Children (2 years of age to 10 years old): 3-5 ml
  - Older Children & Adults: 5-10 ml
  - Autopsy: 2-3 ml unclotted cord or cardiac blood

Specimen Collection and Shipping:
- Ship sample at room temperature for receipt at EGL within 72 hours of collection. Do not freeze.

Related Tests

- Deletion/duplication analysis is available for the CHM gene.
- Custom diagnostic mutation analysis (KM) is available to family members if mutations are identified by targeted mutation testing or sequencing analysis.
- Prenatal testing is available only for known familial mutations to individuals who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.