Microphthalmia with Linear Skin Defects: HCCS Gene Sequencing

Test Code: SHCCS
Turnaround time: 6 weeks
CPT Codes: 81479 x1

Condition Description

Microphthalmia with linear skin defects (MLS) syndrome (OMIM #309801) is characterized by unilateral or bilateral microphthalmia and/or anophthalmia and linear skin defects (areas of aplastic skin), which are usually present at birth and involve the face and neck. Overtime these lesions heal and leave minimal residual scarring. Minor criteria of MLS syndrome include other ocular abnormalities such as microcornea and, central nervous system involvement including agenesis of the corpus callosum and microcephaly, intellectual disability, infantile seizures, and congenital heart defects. Short stature, diaphragmatic hernia, nail dystrophy, hearing loss, and genitourinary malformations may also be present.

MLS syndrome is inherited in an X-linked manner and is usually lethal in males. Most cases present as a single occurrence in a family, however, familial occurrences have been described. Both intra- and interfamilial variability is possible.

Diagnosis is based on clinical findings and the detection of either a chromosomal abnormality that results in monosomy for Xp22 or a mutation in the HCCS gene (Xp22) (OMIM #300056), the only gene known to be associated with MLS syndrome. Approximately 77% of affected individuals have monosomy Xp22 due to either a chromosomal abnormality or an interstitial deletion. Both point mutations and multiple exon deletions of the HCCS gene have been reported.

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

References:
- GeneReviews
- OMIM #309801: MLS syndrome
- OMIM #300056: HCCS gene

Indications

This test is indicated for:
- Confirmation of a clinical diagnosis of MLS syndrome.
- Carrier testing in adults with a family history of MLS syndrome.

Methodology

PCR amplification of 6 exons contained in the HCCS 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: Unknown. 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

* Preferred specimen type: Whole Blood

Type: Whole Blood

Specimen Requirements:
In EDTA (purple top) tube:
Infants (2 years): 3-5 ml
Older Children & Adults: 5-10 ml

Specimen Collection and Shipping: Refrigerate until time of shipment. Ship sample within 5 days of collection at room temperature with overnight delivery.

**Type: Saliva**

Specimen Requirements:

Oragene™ Saliva Collection kit (available through EGL) used according to manufacturer instructions.

Specimen Collection and Shipping: Store sample at room temperature. Ship sample within 5 days of collection at room temperature with overnight delivery.

**Related Tests**

- Deletion/duplication analysis of the HCCS gene by CGH array is available for those individuals in whom sequence analysis is negative.
- 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.
- X-Linked Intellectual Disability panels are available for 30, 60, and 90 genes.