Microphthalmia with Linear Skin Defects: \textit{HCCS} Gene Deletion/Duplication

\textbf{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 \textit{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 \textit{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.

\textbf{References:}

- GeneReviews
  - OMIM \#309801: MLS syndrome
  - OMIM \#300056: \textit{HCCS} gene

\textbf{Genes}

\textit{HCCS}

\textbf{Indications}

This test is indicated for:

- Confirmation of a clinical diagnosis of MLS syndrome in an individual in whom sequence analysis was negative.
- Carrier testing in adults with a family history of MLS syndrome in whom sequence analysis was negative.

\textbf{Methodology}

DNA isolated from peripheral blood is hybridized to a CGH array to detect deletions and duplications. The targeted CGH array has overlapping probes which cover the entire genomic region.

\textbf{Detection}

Detection is limited to duplications and deletions. The CGH array will not detect point or intronic mutations. Results of molecular analysis must be interpreted in the context of the patient's clinical and/or biochemical phenotype.

\textbf{Specimen Requirements}

\textit{Submit only 1 of the following specimen types}

\textbf{Type: Whole Blood (EDTA)}

\textbf{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

\textbf{Specimen Collection and Shipping:}

Ship sample at room temperature for receipt at EGL within 72 hours of collection. Do not freeze.

\textbf{Type: DNA, Isolated}
Specimen Requirements:
Microtainer
3µg
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.

Related Tests
- Sequence analysis of the HCCS gene is available and is required before deletion/duplication analysis.
- 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.