Lynch Syndrome: EPCAM Gene Deletion/Duplication

Test Code: DEPCA
Turnaround time: 2 weeks
CPT Codes: 81403 x1

Condition Description

Deletions of the 3’ end of the EPCAM gene (2q21) (also known as the TACSTD1 gene) cause Lynch syndrome by methylating and inactivating the MSH2 gene. Kovacs et al. (2009) identified deletions of the EPCAM gene in five of 27 families tested that did not have a mutation in the MLH1 or MSH2 genes. The phenotype of individuals with deletions of the EPCAM gene differs slightly from the classic Lynch syndrome phenotype. These individuals tend to be diagnosed with colorectal cancer only. The age at disease onset (25-63 years) is similar to those with mutations of the MSH2 gene.

Lynch syndrome, caused by a germline mutation in a mismatch repair gene or associated with tumors exhibiting MSI, is characterized by an increased risk of colon cancer and other cancers (e.g., of the endometrium, ovary, stomach, small intestine, hepatobiliary tract, upper urinary tract, brain, skin). Individuals with Lynch syndrome have an approximately 80% lifetime risk for colon cancer. The average age of colorectal cancer diagnosis is 61 years.

The diagnosis of Lynch syndrome can be made on the basis of the Amsterdam Clinical Criteria or by molecular genetic testing for germline mutations in one of several mismatch repair (MMR) genes. The Amsterdam Criteria, first established in 1990 for research purposes, were later modified to include the other Lynch syndrome-related cancers for clinical diagnostic purposes. The Amsterdam Criteria are 1) Three or more family members, one of whom is a first-degree relative of the other two, with a confirmed diagnosis of colorectal cancer 2) Two successive affected generations 3) One or more colorectal cancers diagnosed before age 50 years. The modified Amsterdam Criteria replace "colorectal cancer" with "any Lynch syndrome-related cancers." The sensitivity and specificity of the Amsterdam Criteria for identifying a mutation in the mismatch repair genes MSH2 and MLH1 have been reported to be 61% and 67%, respectively. The sensitivity is increased to 78% using the modified Amsterdam Criteria. However, broadening the criteria decreases the specificity.

Individuals at-risk for Lynch syndrome due to family history.

Confirmation of a clinical diagnosis of Lynch syndrome.

Individuals at-risk for Lynch syndrome due to family history.

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.

Detection

Kovacs et al. (2009) identified deletions of the EPCAM gene in five of 27 families tested that did not have a mutation in the MLH1 or MSH2 genes. 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.

References:

- GeneReviews
- OMIM #185535: EPCAM gene
- OMIM #120435: Lynch syndrome

Genes

EPCAM

Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of Lynch syndrome.
- Individuals at-risk for Lynch syndrome due to family history.

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Specimen Requirements

Submit only 1 of the following specimen types

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.

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

- Sequence analysis of the MLH1, MSH2, MSH6, and PMS2 genes is available as a panel or individually.
- Deletion/duplication analysis of the MLH1, MSH2, and MSH6 genes is available as a panel or individually for those individuals in whom sequence analysis is negative.
- Immunohistochemistry for the MLH1, MSH2, MSH6, and PMS2 proteins is available individually.
- Microsatellite instability testing is available and is recommended before immunohistochemistry.