

Li-Fraumeni Syndrome: *TP53* Gene Deletion/Duplication

Test Code: QY

Turnaround time: 2 weeks

CPT Codes: 81228 x1

Condition Description

Li-Fraumeni Syndrome (LFS) is an autosomal dominant cancer predisposition syndrome associated with soft-tissue sarcoma, breast cancer, leukemia, osteosarcoma, melanoma, and cancer of the colon, pancreas, adrenal cortex, and brain [1]. Tumors frequently appear in childhood and affected individuals may experience multiple primary tumors during their lifetime. The cancer risk is estimated to be 90% by age 60.

Classic LFS is defined as a proband with a sarcoma before the age of 45 years and a first-degree relative with any cancer before the age of 45 years, and one additional first- or second-degree relative in the same lineage with any cancer before the age of 45 years or a sarcoma at any age.

Li-Fraumeni-Like Syndrome (LFL) is defined alternately as a proband with any childhood cancer, or a sarcoma, brain tumor, or adrenocortical tumor before the age of 45 years, plus a first- or second-degree relative in the same lineage with a typical LFS tumor at any age, and an additional first- or second-degree relative in the same lineage with any cancer before the age of 60 years (Birch [2]); or two first- or second-degree relatives with any LFS-related cancer at any age (Eeles [3]).

The *TP53* gene (17p13.1) has 10 exons and is a tumor suppressor gene. Approximately 70% of LFS cases and 40% of LFL cases contain germline mutations in *TP53*. 95% of mutations can be detected by sequence analysis. Some genotype-phenotype correlations have been found: brain tumors seem to be associated with missense *TP53* mutations located in the DNA-binding loop that contact the minor groove of DNA, whereas adrenal gland carcinomas are associated with missense mutations located in the loops opposing the protein-DNA contact surface. In addition, mutations likely to result in a null phenotype (absence of the protein or loss of function) are associated with earlier onset brain tumors. A few families with LFS or LFL have been found to have mutations in the *CHEK2* gene. The specific contribution of *CHEK2* mutations to LFS and LFL-associated cancer risks has yet to be defined.

Sequencing of the *TP53* gene is recommended after a clinical diagnosis consistent with Li-Fraumeni Syndrome, and provides a complementary method to confirm the presence of mutations in a proband, identify at-risk individuals among the proband's relatives, and provide prenatal diagnosis in families with known mutations.

For patients with suspected LFS or LFL, 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.

Please [click here](#) for the GeneTests summary on this condition.

References:

- Li FP, Fraumeni JF Jr. Soft-tissue sarcomas, breast cancer, and other neoplasms. A familial syndrome. *Ann Intern Med.* 1969; 71: 747-752.
- Birch JM, Hartley AL, Tricker KJ, Prosser J, Condie A, Kelsey AM, Harris M, Jones PH, Binchy A, Crowther D. et al. Prevalence and diversity of constitutional mutations in the p53 gene among 21 Li-Fraumeni families. *Cancer Res.* 1994; 54: 1298-1304.
- Eeles RA. Germline mutations in the TP53 gene. *Cancer Surv.* 1995; 25: 101-124.

Genes

[TP53](#)

Indications

This test is indicated for:

- Confirmation of a suspected diagnosis of LFS or LFL in an individual in whom sequence analysis was negative.
- Individuals at risk for LFS or LFL due to family history in whom sequence analysis was negative.

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

Detection is limited to duplications and deletions. Array CGH will not detect point mutations or intronic mutations. The frequency of deletion/duplication mutations in LFS and LFL is unknown.

Results of molecular analysis must be interpreted in the context of the patient's clinical presentation and family history.

Specimen Requirements

Submit only 1 of the following specimen types

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.

Type: DNA, Isolated

Specimen Requirements:

Microtainer

3µg

Isolation using the Perkin Elmer™ Chemagen™ 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.

Special Instructions

Please submit copies of pedigree or other family history information along with the sample. Contact the laboratory if further information is needed. Sequence analysis is required before deletion/duplication analysis by targeted CGH array. If sequencing is performed outside of EGL Genetics, please submit a copy of the sequencing report with the test requisition form.

Related Tests

- Sequence Analysis of *TP53* gene is available and is required before deletion/duplication analysis
- Prenatal testing is available to individuals who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.