Li-Fraumeni Syndrome (TP53)

**Background:** Li-Fraumeni syndrome (OMIM 151623) is an autosomal dominant cancer predisposition syndrome that predisposes an affected individual to multiple forms of cancer (breast cancer, soft tissue sarcoma, leukemia, melanoma, osteosarcoma, colon cancer, pancreatic cancer, esophageal cancer, brain tumors, and other malignancies). The syndrome is due to germline mutations in the TP53 gene.

A TP53 germline mutation is suspected to be present in an individual for the following family history:
- a proband with a sarcoma under 45 years of age, and
- a first degree relative with any cancer under 45 years of age, and
- a third family member who is a first- or second-degree relative with cancer under 45 years or a sarcoma at any age.

More than 50% of individuals meeting the above criteria will have an identifiable mutation in the TP53 gene.

**Assay:** Direct mutation analysis by full sequencing of exons 2-11; to date, 95% of mutations have been documented in exons 3-9. Analysis for exonic deletions or duplications by quantitative (real-time) PCR.

**Eligibility** Patients who have one of the index cancers and whose family history meets the Li-Fraumeni criteria are eligible for screening. At-risk individuals from families where a mutation has already been identified are eligible for site-specific mutation testing.

**Utility:** Diagnostic confirmation, carrier detection, and prenatal diagnosis

**Sensitivity:** If the patient’s mutation is in the coding sequencing of the TP53 gene, the testing will detect the mutation ~98% of the time. Mutations in non-coding sequences or other rearrangements will not be detected by full sequencing and deletion/duplication analysis.

**Turnaround:** 5-6 weeks for full sequencing; 4-6 weeks for deletion/duplication analysis; 2-3 weeks for a known familial mutation, and 7-10 days for prenatal diagnosis of known mutation

**Fees:** $840 for full sequencing analysis of exons 2-11
$560 for screening for deletion/duplication
$360 for known familial mutation
$460 for prenatal diagnosis for a known familial mutation (cost includes MCC studies )

**CPT codes:** Full sequencing of exons 2-11: 81405
Screening for deletion/duplication: 81404
Known familial mutation: 81403
Prenatal diagnosis: 81403, 81265