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Test Update 778

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Test Name POLE Mutation
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NEW TEST

POLE Mutation

Order Code:	POLE
CPT Code:	81479, 88381

Effective October 6, 2021 MLabs will offer *POLE* Mutation testing.

Test Usage: DNA polymerase epsilon, encoded by the *POLE* gene, is involved in DNA replication and repair. Somatic *POLE* mutations, primarily affecting the exonuclease domain and proofreading capability of this polymerase, are present in approximate 5-16% of endometrial carcinomas and define a subgroup with numerous mutations ('ultramutated'; ≥ 100 mutations/Mb), enhanced immune response and excellent clinical outcomes. Somatic *POLE* mutations are also present in 1-2% of colorectal carcinomas. Endometrial carcinomas with pathogenic *POLE* mutations have thus been codified as a distinct clinical entity according to the National Comprehensive Cancer Network (NCCN) guidelines . The most common *POLE* mutations include P286R, V411L, S297F, A456P and S459F. However, a wide variety of other, less common *POLE* variants have been described including some that are not associated with the 'ultramutated' genomic signature or whose potential pathogenicity is not known. Germline *POLE* mutations – particularly L242V – are also described and are associated with polymerase proofreading-associated polyposis syndrome (PPAP). If there is a clinical suspicion of germline *POLE* mutation, *POLE* sequencing of peripheral blood is recommended.

This DNA based test is performed by Sanger Sequencing of *POLE* exons 9, 11, 13 and 14 (NM_006231). The limit of detection of this assay is 50% mutation-bearing cells.

Collection Instructions: For formalin-fixed, paraffin-embedded tissue, a block containing an area with a high percentage of neoplastic cells (for micro-/macro-dissection) is preferred. Unstained, UNBAKED slides (5-8, 10-micron slides; 10-15 if few neoplastic cells are present) with associated H&E-stained slide are also acceptable. Decalcified tissue or other fixatives will be accepted and the assay attempted; however, these may result in failed testing due to degraded nucleic acid. Both blocks and slides should be stored at room temperature. A Diff-Quik or Papanicolaou stained aspirate smear (preferably containing a high percentage and overall number of neoplastic cells) is also acceptable. Store at room temperature.

Alternate Specimen

For exhausted formalin-fixed, paraffin-embedded blocks, the original Hematoxylin and Eosin-stained slide(s) may be extracted at the discretion of the extracting pathologist. The extraction process will result in destruction of these slide(s); however, a digital image of the slide(s) must be collected prior to extraction and retained for a minimum of 10 years from the specimen collection date.

Previously extracted DNA from a CLIA certified laboratory may be accepted; however, the extracting laboratory must take responsibility for ensuring that viable, neoplastic cells comprise at least 50% of cellularity within the extracted sample.

Analytic Time: 3-10 days

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