

MayoComplete Endometrial Carcinoma Panel, Next-Generation Sequencing, Tumor

Patient ID SA00174987	Patient Name TESTINGRNV, ABNORMAL	Birth Date 1988-02-18	Sex F	Age 37
Order Number SA00174987	Client Order Number SA00174987	Ordering Physician CLIENT,CLIENT	Report Notes	
Account Information C7028846 DLMP Rochester		Collected 28 Mar 2025 00:00		

MayoComplete Endometrial Panel

Result

MCR

Provided diagnosis: endometrial carcinoma

Microsatellite Instability (MSI) status: Stable (MSS)

The following CLINICALLY RELEVANT VARIANT was detected:

Gene: TP53

DNA Change: c.641A>G (Exon 6)

Amino Acid Change: p.H214R (His214Arg)

Variant Allele Frequency: 64.9%

The following VARIANT OF UNCERTAIN SIGNIFICANCE was detected:

Gene: CTNNB1

DNA Change: c.1624C>T (Exon 10)

Amino Acid Change: p.R542C (Arg542Cys)

Variant Allele Frequency: 59.9%

No other reportable sequence variants were detected within the analyzed regions of the tested gene(s) listed in the method description.

This test does not include NTRK fusion testing. Clinically approved therapy is available for patients with metastatic or unresectable solid tumors with an NTRK fusion [fda.gov/drugs]. If clinically indicated, consider NTRK Gene Fusion Panel (NTRK) for evaluation of NTRK fusions. Please refer to mayocliniclabs.com or call 1 800-533-1710 for more information.

Interpretation

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MSI: Stable (MSS)

NO evidence of microsatellite instability was detected suggesting the presence of normal DNA mismatch repair function within the tumor. Current data suggest that advanced stage solid tumors with intact mismatch repair (MSS) are less likely to be responsive to treatment with immunotherapies such as anti-PD-1 therapies

[PMID 28596308, PMID 29355075].

However, lenvatinib in combination with pembrolizumab has been FDA-approved for patients with advanced endometrial carcinoma with intact mismatch repair (MSS) and who have disease progression following prior systemic therapy but are not candidates for curative surgery or radiation [PMID: 32167863, PMID: 32295834].

1) TP53 c.641A>G (p.H214R) (Exon 6)

The TP53 gene encodes the tumor suppressor p53, a protein that is involved in the DNA damage cell cycle checkpoint and causes cell cycle arrest when it senses DNA damage. p53 can also activate DNA repair genes or induce apoptosis in the presence of DNA damage. Alterations in TP53 typically result in a loss of p53 protein function. Additionally, some alterations are predicted to have oncomorphic or gain-of-function properties leading to downstream oncogenic effects, including genomic instability and excessive cell proliferation [PMID:9039259, PMID:15625370, PMID:11400116, PMID:12826609, PMID:21760960, PMID:18802452].

TP53 mutations have been reported in 9–11% of endometrial cancer samples and define a molecular subclass of endometrial carcinoma [COSMIC, cBioPortal for Cancer Genomics, PMID: 33602681, PMID: 32296930, PMID: 33806979].

The presence of TP53 mutations in both solid tumors and hematologic malignancies is associated with tumor aggressiveness and poor survival [PMID: 35444210, PMID: 16861262, PMID: 2887079, PMID: 2297721, PMID: 35561299].

There are currently no known clinically approved therapies that specifically target TP53 mutations.

VARIANT OF UNCERTAIN SIGNIFICANCE

One variant of uncertain significance was detected. The variant was not observed at significant frequency in population germline/cancer somatic variant databases nor predicted to be functionally significant based on variant type/in silico algorithm results. Additionally, there was no convincing published evidence of cancer association. Therefore, the clinical significance of the

Performing Site Legend

Code	Laboratory	Address	Lab Director	CLIA Certificate
MCR	Mayo Clinic Laboratories - Rochester Main Campus	200 First Street SW, Rochester, MN 55905	Nikola Baumann Ph.D.	24D0404292

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detected variant is unknown.

Additional Information

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CLINICAL TRIALS

Possible clinical trials of benefit for this patient can be found at the following sites:

- 1) ClinicalTrials.gov:
www.clinicaltrials.gov/ct2/search/advanced
- 2) Mayo Clinic: www.mayo.edu/research/clinical-trials/
- 3) National Cancer Institute: www.cancer.gov/clinicaltrials/search

REFERENCE TRANSCRIPTS

Sequence variant nomenclature is based on the following RefSeq accession numbers (build GRCh37 (hg19)): CTNNB1 NM_001904 and TP53 NM_000546.

Specimen

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Tissue, Tumor

Tissue ID

MCR

12345

Method

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Microscopic examination is performed by a pathologist to identify areas of tumor for enrichment by macrodissection.

Next generation sequencing is performed to test for the presence of microsatellite instability and a mutation within most coding regions and exon/intron boundaries of the following genes: ATM, ATR, BRCA1, BRCA2, CDK12, CTNNB1, EPCAM, ERBB2, FBXW7, L1CAM, MLH1, MSH2, MSH6, NBN, PALB2, PMS2, POLE, PPP2R1A, and TP53

Variant nomenclature is based on build GRCh37 (hg19). For details about gene transcripts (RefSeq accession numbers), specific targeted regions of each gene, and additional information on this test, see www.mayocliniclabs.com (Test ID MCECP).

Disclaimer

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This test cannot differentiate between somatic and germline alterations. Additional testing may be necessary to clarify the significance of results if there is a potential hereditary risk.

DNA variants of uncertain significance may be identified.

A negative result does not rule out the presence of a variant that may be present but below the limits of detection of this assay. The analytical sensitivity of this assay for sequence reportable alterations is 5% mutant allele frequency with a minimum coverage of 500X in a sample with at least 20% tumor content.

Point mutations and small insertion/deletion mutations will be detected in the ATM, ATR, BRCA1, BRCA2, CDK12, CTNNB1, EPCAM, ERBB2, FBXW7, L1CAM, MLH1, MSH2, MSH6, NBN, PALB2, PMS2, POLE, PPP2R1A, and TP53 genes only. This test may detect single exon deletions but does not detect multi-exon deletions, duplications, larger-scale genomic copy number variants, copy neutral loss of heterozygosity (LOH), or epigenetic modifications such as promoter methylation. DELINS of 1,000 bp or less are detectable with at least 50 or more supporting reads.

This test cannot reliably determine if a variant identified in PMS2 exons 11–15 originated from PMS2 or the highly homologous pseudogene PMS2CL. In the instance that a reportable variant is detected in PMS2 exons 11–15, additional testing will be recommended in the patient report.

Variant allele frequency (VAF) is the percentage of sequencing reads supporting a specific variant divided by the total sequencing reads at that position. In somatic testing, VAF should be interpreted in the context of several factors including, but not limited to: tumor purity/heterogeneity/copy number status (ploidy, gains/losses, loss of heterozygosity) and sequencing artifact/misalignment [PMID: 27144058, PMID: 29769535].

Rare polymorphisms may be present that could lead to false-negative or false-positive results.

The presence or absence of a variant may not be predictive of response to therapy in all patients.

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Test results should be interpreted in the context of clinical, tumor sampling, histopathological, and other laboratory data. If results obtained do not match other clinical or laboratory findings, contact the laboratory for discussion. Misinterpretation of results may occur if the information provided is inaccurate and/or incomplete.

Reliable results are dependent on adequate specimen collection and processing. This test has been validated on cytology slides

and formalin-fixed, paraffin-embedded tissues; other types of fixatives are discouraged. Improper treatment of tissues, such as decalcification, may cause PCR failure.

Released By MCR
Katherine B. Geiersbach, M.D.

Received: 29 Mar 2025 12:18 **Reported:** 30 Apr 2025 17:58

Laboratory Notes

- 1 This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.

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