

Patient ID SA00174989	Patient Name TESTINGRNV, ABNORMAL	Birth Date 1974-02-18	Sex F	Age 51
Order Number SA00174989	Client Order Number SA00174989	Ordering Physician CLIENT,CLIENT	Report Notes	
Account Information C7028846 DLMP Rochester		Collected 28 Mar 2025 00:00		

MayoComplete Fibromyomatous RCC

Result

MCR

Provided diagnosis: renal cell carcinoma

The following CLINICALLY RELEVANT VARIANT was detected:

Gene: TSC2

DNA Change: c.5160+2dup

Variant Allele Frequency: 17.5%

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

Interpretation

MCR

1) TSC2 c.5160+2dup

TSC2 encodes tuberlin, which forms a heterodimer with hamartin (encoded by TSC1) to act as a GTPase activating protein for Rheb, a potent activator of the mammalian target of rapamycin (mTOR) [PMID:12271141, PMID:12869586, PMID:12906785]. By converting Rheb from a GTP- to GDP-bound state, the hamartin/tuberlin heterodimer inactivates Rheb and suppresses mTOR activity [PMID:18466115, PMID:21428921]. Inactivation of TSC2, mainly through deletions and mutations, leads to activation of the mTOR signaling pathway and contributes to tumorigenesis [PMID:12271141, PMID:16452213].

TSC2 mutations have been reported in 2–3% of renal tumor samples [COSMIC, cBioPortal for Cancer Genomics].

TSC2 mutations are described in the literature in new and emerging renal entities including renal cell carcinoma with fibromyomatous stroma, eosinophilic solid and cystic renal cell carcinoma, eosinophilic vacuolated tumor, low grade oncocytic tumor, and angiomyolipoma [PMID: 33526874, PMID: 34531523, PMID: 34521993]. The presence of this alteration in this specimen should be interpreted in correlation with histopathological and clinico-radiological findings.

The loss of TSC2 function has been reported to lead to activation

of mTOR, suggesting that TSC2 loss or Tuberlin inactivation may predict sensitivity to mTOR inhibitors [PMID:12869586, PMID:12906785]. In a number of cancer types (including bladder, breast, thyroid, and PEComa), patients who have had exceptional responses to mTOR inhibitors have been found to harbor TSC1 or TSC2 inactivating alterations [PMID:22923433, PMID:25295501, PMID:20048174, PMID:22927055, PMID:26859683]. However, additional studies are needed to assess the efficacy of these therapies in solid tumors.

Additional Information

MCR

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 TRANSCRIPT

Sequence variant nomenclature is based on the following RefSeq accession number (build GRCh37 (hg19)): TSC2 NM_000548.

Specimen

MCR

Tissue, Tumor

Tissue ID

MCR

12345

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

Patient ID SA00174989	Patient Name TESTINGRNA, ABNORMAL	Birth Date 1974-02-18	Sex F	Age 51
Order Number SA00174989	Client Order Number SA00174989	Ordering Physician CLIENT, CLIENT	Report Notes	
Account Information C7028846 DLMP Rochester		Collected 28 Mar 2025 00:00		

Method

MCR

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 a mutation within most coding regions and exon/intron boundaries of the following genes: ELOC, TSC1, TSC2, and VHL.

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 MCFRC).

Disclaimer

1 MCR

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 ELOC, TSC1, TSC2, and VHL 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.

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.

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

Sounak Gupta, M.B.B.S., Ph.D.

Received: 29 Mar 2025 12:22

Reported: 02 May 2025 08:03

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.

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