Patient ID	Patient Name		Birth Date	Sex	Age
SA00174971	TESTINGRNV, ABNORMAL		1984-01-06	F	41
Order Number	Client Order Number	Ordering Physician	Report Notes		
SA00174971	SA00174971	CLIENT,CLIENT			
Account Information		Collected			
C7028846 DLMP Rochester		28 Mar 2025 00:00			

DICER1 Mutation Analysis, Tumor

Result

MCR

Provided diagnosis: uterine embryonal rhabdomyosarcoma

The following CLINICALLY RELEVANT VARIANTS were detected:
Gene: DICER1
DNA Change: c.5439G>C (Exon 25)
Amino Acid Change: p.E1813D (Glu1813Asp)
Variant Allele Frequency: 32.1%

Gene: DICER1
DNA Change: c.5096–1G>T
Variant Allele Frequency: 46.3%

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

Interpretation

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1) DICER1 c.5439G>C (p.E1813D) (Exon 25) and c.5096–1G>T

DICER1 encodes Dicer1, a candidate tumor suppressor gene that plays a key role in miRNA biogenesis, thereby regulating gene expression [PMID:23222681, PMID:25176334, PMID:11201747]. The role of DICER1 in cancer may be context-dependent, as DICER1 inactivation has been associated with tumorigenesis in some tumor types, whereas increased DICER1 mRNA or Dicer1 protein expression has been associated with metastasis and invasion in other tumor types [PMID:17401365, PMID:21698147, PMID:22331912, PMID:17071602, PMID:19903759].

Among female genital tract tumors, DICER1 mutations are a diagnostic marker of embryonal rhabdomyosarcoma and Sertoli-Leydig cell tumors [PMID: 34996131, PMID: 31900434, PMID: 22187960,PMID: 33846547, PMID: 24675358]. DICER1 mutations also occur in the context of DICER1 tumor predisposition syndrome, a hereditary cancer predisposition syndrome associated with increased risk for development of pleuropulmonary blastoma, cystic nephroma, Wilms' Tumor, anaplastic sarcoma of the kidney, ovarian Sertoli-Leydig cell tumor, cervical embryonal rhabdomyosarcoma, pineoblastoma, and pituitary blastoma [PMID: 34599283]. In addition, in central nervous system (CNS) tumors, DICER1 mutations are a diagnostic molecular biomarker for primary intracranial sarcoma, DICER1-mutant, embryonal tumor with multilayered rosettes, and pituitary blastoma [WHO Classification of Tumours Editorial Board. Central nervous system tumours. Lyon (France): International Agency for Research on Cancer, 5th ed., vol. 6, 2021].

Additional studies are needed in order to assess the clinical implications of DICER1 testing in other neoplasms.

Germline (inherited) mutations in DICER1 are associated with a hereditary cancer syndrome. This test does not distinguish between germline and somatic (not inherited) genetic variants. If a hereditary cancer syndrome is suspected for this patient, clinical correlation with their personal and family history as well as a referral for genetic counseling is recommended.

There are currently no known clinically approved therapies that specifically target DICER1 mutations.

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)): DICER1 NM_177438.

Specimen

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Tissue, Tumor

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	Patient Name		Birth Date	Sex	Age
SA00174971	TESTINGRNV, ABNORMAL		1984-01-06	F	41
Order Number	**Client Order Number**	**Ordering Physician**	**Report Notes**		
SA00174971	SA00174971	CLIENT,CLIENT			
Account Information		**Collected**			
C7028846 DLMP Rochester		28 Mar 2025 00:00			

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. DNA is extracted from FFPE or cytology slides, and next generation sequencing is performed to evaluate the presence of a mutation in all coding regions and exon/intron boundaries of the DICER1 gene

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 DICET).

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 DICER1 gene 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

Katherine B. Geiersbach, M.D.

Received: 29 Mar 2025 10:11 **Reported:** 08 Apr 2025 15:16

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

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MCR	Mayo Clinic Laboratories - Rochester Main Campus	200 First Street SW, Rochester, MN 55905	Nikola Baumann Ph.D.	24D0404292