

Patient ID SA00174975	Patient Name TESTINGRNV, ABNORMAL	Birth Date 1983-01-09	Sex F	Age 42
Order Number SA00174975	Client Order Number SA00174975	Ordering Physician CLIENT, CLIENT	Report Notes	
Account Information C7028846 DLMP Rochester		Collected 28 Mar 2025 00:00		

Histone Genes Mutation Analysis, Ts

Result

MCR

Provided diagnosis: bone lesion

The following CLINICALLY RELEVANT VARIANT was detected:

Gene: H3-3B (previously H3F3B)

DNA Change: c.110A>T (Exon 2)

Amino Acid Change: p.K37M (Lys37Met) (also known as K36M)

Variant Allele Frequency: 16.1%

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) H3-3B c.110A>T (p.K37M) (also known as K36M) (Exon 2)

H3-3B, also known as H3F3B, encodes the replacement variant histone H3.3, which is associated with replication-independent deposition machinery and the promoter regions of transcriptionally active genes; variant histone H3.3 is the most common form of histone H3 in differentiated cells [PMID:12086617, PMID:14718166, PMID:15006351, PMID:15776021]. Via interaction with ATRX protein and Daxx, histone variant H3.3 has also been reported to impact alternative lengthening of telomeres (ALT) processes, with phosphorylated H3.3 having been associated with preservation of chromatin integrity and cell survival [PMID:20651253, PMID:25690891].

H3-3B mutations primarily involve codon K37 (also known as K36) and K28 (also known as K27) which are located in a critical post-translational modifiable region of the N-terminal histone tail. They lead to oncogenic reprogramming of the epigenetic landscape and impact gene expression [PMID:24162739].

H3-3B mutations are a molecular biomarker in multiple tumor types, including chondroblastoma [PMID: 24162739].

The PRESENCE of a mutation in H3-3B supports the diagnosis of any of these tumor types and should be interpreted in correlation with histopathological and clinico-radiological findings

and other genetic test results.

There are currently no known clinically approved therapies that specifically target H3-3B 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 TRANSCRIPT

Sequence variant nomenclature is based on the following RefSeq accession number (build GRCh37 (hg19)): H3-3B NM_005324.

Specimen

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Tissue, Tumor

Tissue ID

MCR

12345

Method

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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: H3-3A, H3-3B, H3C2, H3C3, and H3C14.

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 HISGT).

Disclaimer

1 MCR

This test cannot differentiate between somatic and germline

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 SA00174975	Patient Name TESTINGRNA, ABNORMAL	Birth Date 1983-01-09	Sex F	Age 42
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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 H3-3A, H3-3B, H3C2, H3C3, and H3C14 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

Katherine B. Geiersbach, M.D.

Received: 29 Mar 2025 10:37

Reported: 08 Apr 2025 15:19

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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