Abdul Cader Mohamed Razick

AGE: 69 years | **Gender:** Male | **Coupon/UID:** NA **/** AOM0306

Diagnosis: Colorectal Neoplasms

MEDGENOME

MGM2529 : Colorectal advanced panel by NGS & Microsatellite Instability (MSI) by fragment analysis

Report Details		Specimen Information		Ordering Clinician	
Sample ID / Order ID:	9639894 / 1569213	**Specimen Site:**	Colon	**Clinician:**	Dr. Mahendra Perera
Collection Date:	25th November 2025	**Specimen Received:**	FFPE Tissue Blocks [2]	**Affiliation:**	Aegle Omics Private Limited
Date Received:	22nd December 2025	**Specimen Tested:**	YK34563L	**Serviced By:**	18718
Report Date & Time:	8th Jan 2026 18:16 PM	**Tumor Content (%):**	55	**Report Status:**	Final

Clinical Summary:

Moderately differentiated infiltrating adenocarcinoma of sigmoid colon; T4N1bM0.

TEST RESULT SUMMARY

Microsatellite Instability (MSI) Test

Status - Stable

Kindly refer to the complete MSI reports below.

Next Generation Sequencing (NGS) Results

POSITIVE

Gene	Findings	Gene	Findings
AKT1	Not Detected	*APC*	Not Detected
BRAF	Not Detected	*ERBB2*	Not Detected
HRAS	Not Detected	*KRAS*	**G12D**
MET	Not Detected	*NRAS*	Not Detected
NTRK1	Not Detected	*NTRK2*	Not Detected
NTRK3	Not Detected	*PIK3CA*	Not Detected
PIK3R1	Not Detected	*POLD1*	Not Detected
POLE	Not Detected	*PTEN*	Not Detected
RET	Not Detected	*SMAD4*	Not Detected
TP53	Not Detected		

Please refer to the complete variant details in the result table in page 2.

Next Generation Sequencing (NGS) Test Result

Result - POSITIVE
CLINICALLY RELEVANT VARIANT/S DETECTED

AMP Classification ^	CDS variant details	Interpretation	Treatment Recommendations	$Treatment Response
***KRAS* p.Gly12Asp (MISSENSE)** Variant Allele Frequency - 23.6%				
Tier I	c.35G>A (ENST00000311936.8)	Oncogenic	Anti-EGFR monoclonal antibodies	Ineffective

No clinically significant fusion has been detected in this sample

^Refer to Glossary section for the classification criteria details.

$Drug Approvals are based on US-FDA Guidelines. Kindly refer to local guidelines if required.

ADDITIONAL BIOMARKERS DETECTED

This section provides information about variants that do not have any therapeutic value. However, these variants may or may not have a likely oncogenic effect.

No other biomarkers that warrants to be reported was detected

ACTIONABLE BIOMARKER DETAILS

KRAS (p.Gly12Asp) - MISSENSE

Gene: *KRAS*	**Exon:** 2	**Variant Allele Frequency:** 23.6%
Nucleotide change: chr12:g.25245350C>T	**Protein change:** p.Gly12Asp	**Population MAF:** 0 (1000G);0.001314(gnomAD);
cDNA change: c.35G>A	**Variant Type:** MISSENSE	**In-silico Predictions:** D_lc(SIFT); D(LRT); NA(Polyphen2)
Transcript ID: ENST00000311936.8	**Variant Allele Depth/Total depth:** 126/534x	**Gene Function:** Oncogene

Gene Summary: *KRAS*, a Kirsten ras oncogene homolog from the mammalian ras gene family, encodes a protein that is a member of the small GTPase superfamily. A single amino acid substitution is responsible for an activating mutation. The transforming protein that results is implicated in various malignancies, including lung adenocarcinoma, mucinous adenoma, ductal carcinoma of the pancreas and colorectal carcinoma. Alternative splicing leads to variants encoding two isoforms that differ in the C-terminal region.

Clinical and Therapeutic Relevance: The small GTPase*KRAS*activates the RAS/MAPK signaling pathway to promote cell proliferation and survival. Variants at codon 12 within*KRAS* exon 2 have been shown to promote transformation due to enhanced downstream signaling. **Clinical studies have established that metastatic colorectal cancers (CRC) with mutations at this codon show resistance to the anti-EGFR antibodies cetuximab and panitumumab.**Three out of seven CRC patients treated with PLK1 inhibitor onvansertib (nms-1286937) and combined with FOLIFRI/bevacizumab achieved a partial response (PR), and three had stable disease (SD). In a CRC cell line harboring the BRAF.V600E mutation, this variant conferred resistance to the combination treatment of cetuximab with BRAF inhibitor vemurafenib, dabrafenib, or encorafenib, or the triple combination of encorafenib, cetuximab, and PIK3 inhibitor alpelisib. However, the same cell model was sensitive to combination treatment with MEK inhibitor selumetinib and cetuximab, MEK inhibitor trametinib and dabrafenib, or a triple combination of trametinib, dabrafenib, and cetuximab. Other CRC cell lines with this mutation showed resistance to EGFR inhibitor neratinib but sensitivity to trametinib.

PubMed References: 38231047, 35913398, 27312529, 26989027, 26243863, 24024839, 22169769, 39133932, 39133921, 35797463, 33579957, 31088841, 30194935

AMP-ASCO-CAP CLASSIFICATION CRITERIA

Genetic test results are reported based on the somatic variant classification recommendations of College of American Pathologists (CAP) /American society for Clinical Oncology (ASCO)/Association of Molecular Pathologists (AMP) [PMID: 27993330] as described in the table below:

Tier	Criteria
Tier I	Variants of strong clinical significance.
Tier II	Variants of potential clinical significance.
Tier III	Variants of unknown clinical significance
Tier IV	Benign or likely benign variants

DISCLAIMER

- **Decisions regarding treatment action plans should not be solely based on these test results. These findings are highly recommended to be correlated with the patient's clinical, pathological, radiological and family history for decisions on diagnosis, prognosis, or therapeutics.**
- The therapy information provided in this report is based on FDA approved drugs data, NCCN guidelines, peer reviewed published literature, standard clinical databases, and strength of biomarker results till date. These therapies may or may not be suitable/beneficial to a particular patient. This clinical report summarises potentially effective medications, potentially ineffective medications, and medications that may pose a higher risk of adverse reactions by mapping the patient's genetic alterations to the biomedical reference information. The report may also provide prognostic and diagnostic biomarkers detected or shown for the given disease context.The treatment recommendations for the variants classified in Tier II are not provided.
- The clinical trials information provided in this report is compiled from www.clinicaltrials.gov as per currently available data, however completeness of information provided herein cannot be guaranteed. This information should only be used as a guide and specific eligibility criteria should be reviewed thoroughly for the concerned patient. MedGenome Labs does not guarantee or promise an enrolment in any clinical trials.
- The identification of a genomic biomarker does not necessarily imply pharmacological effectiveness or ineffectiveness. The medications identified by the treating physician may or may not be suitable for use on a particular patient. Thus, the clinical report does not guarantee that any particular agent will be effective in the treatment of any particular condition. Also, the absence of a treatment option does not determine the effectiveness or predict an ineffective or safety-relevant effect of a medication selected by the treating physician.
- The classification and clinically relevant information for the reported variants is based on peer-reviewed publications, public clinical databases, medical guidelines (NCCN, ASCO, AMP) or other publicly available information and it has been ensured that the information provided is up to date at the time of report generated, however continuous updates may happen in public domains. Also, the classification of variants can change based on the updated literature evidence. Re-analysis of the results can be requested at additional cost.
- This test is performed on the patient's tumor sample without a paired blood sample; therefore, it may include variations which may be of germline origin. However, this test is designed and validated for the detection and reporting of somatic genomic variants only and does not discriminate between germline and somatic variants. If clinically warranted, appropriate germline testing and genetic counselling for the patient should be considered for further evaluation.
- **Due to poor quality of FFPE tissue blocks, the QC parameters for extracted RNA may not pass to proceed further with the testing, therefore there is a possibility of assay failure at various steps (RNA QC, Library QC, Bioinformatics QC) or compromised results that include low gene coverage and low variant depth.** However, sample status in such scenarios shall be sent through mail to the ordering clinician.
- This test has been validated at MedGenome Labs and the limit of detection (LOD) of allele fraction for SNVs and InDels is ≥5% and for fusions is ≥10 spanning reads. However, the report may include, at the discretion of laboratory director, the variants with lower allele

burden (3-5%) having strong or potential clinical significance or those have been reported earlier in the patient. Variants with <1% allele fraction and variants of uncertain significance with <5% allele fraction are not routinely reported. However, possibility of false negative or false positive below the limit of detection of this assay cannot be ruled out.

- Large deletions and deep intronic variations are not detected in this assay.
- Copy Number Variations (CNVs) are based on the RNA expression data using a CNV prediction model developed with control samples. Hence, the chromosome coordinates and size of the CNV can not be determined. It is recommended to confirm the CNVs by alternate methods, such as FISH as the sensitivity of NGS for detecting CNVs is not 100%.
- **Additional case specific disclaimer :Although the panel coverage is >95%, the average depth of *POLD1, HRAS, AKT1 & ERBB2* genes are below the reporting criteria. Hence, possibility of false negative result cannot be ruled out. Kindly correlate clinically.**

TEST DESCRIPTION

The MedGenome's Colorectal panel is a high throughput next-generation sequencing assay covering key genes to detect SNVs, InDels, CNVs and fusions and aids in diagnosis, prognosis and therapeutics of the colorectal cancer patients.

TEST METHODOLOGY

Sample type: FFPE Specimen; A histopathologic review is performed to determine the tumor content in the FFPE block/curls.

Extraction and Library Preparation: Tumor nucleic acid is extracted from FFPE (Formalin fixed) tissue block and used to perform targeted gene capture using a custom hybrid capture kit.

Sequencing: The QC passed libraries are sequenced to a minimum depth of 250X on validated Illumina sequencing platform.

Data Analysis: The sequences are processed using a customized and validated analysis pipeline designed to accurately detect all classes of genomic alterations (SNVs, InDels, CNVs and Fusions).

Variant Annotation and Reporting: The variants are annotated using our in-house annotation pipeline. Reportable genomic alterations and fusions are prioritized, classified, and reported based on AMP-ASCO-CAP guidelines [PMID: 27993330] and NCCN guidelines.

Limit of Detection (LOD): The LOD for SNVs and InDels is 5% Variant allele Frequency (VAF) and for fusions is >10 spanning reads.

The transcript used for clinical reporting generally represents the canonical transcript (according to Ensembl release 99 human gene model), which is usually the longest coding transcript with strong/multiple supporting evidence. However, clinically relevant variants annotated in alternate complete coding transcripts could also be reported. Variants annotated on incomplete, and nonsense mediated decay transcripts are not reported.

§This test is developed, and its performance characteristics is determined by MedGenome Labs Ltd.

GENES ANALYSED

SNVs/InDels							
AKT1	*APC*	*BRAF*	*ERBB2*	*HRAS*	*KRAS*	*MET*	*NRAS*
POLE	*POLD1*	*PIK3R1*	*PIK3CA*	*PTEN*	*SMAD4*	*TP53*	

Note: *MET* exon 14 skipping mutations included.

CNVs	
ERBB2	*MET*

FUSIONS				
MET	*NTRK1*	*NTRK2*	*NTRK3*	*RET*

CLINICAL TRIALS

The following trials are potentially best suited for your patient's indication, considering all reported treatment recommendations. See https://clinicaltrials.gov (clinical trials from NCT) or https://trialsearch.who.int (clinical trials from other registries) for more information.

Clinical trials in total : 0 **Trial countries :** IN-India, US-United States

S.No	Title	Phase and ID	Intervention	Disease	Age & Sex
No Clinical Trials.					

Aparna Natarajan, Ph.D
Lead - Genome Analyst (Oncology)

Dr. Syed Muqlisur Rehman, MD Path
Molecular Pathologist
KMC Registration No. 71468

END OF REPORT

Abdul Cader Mohamed Razick

AGE: 69 years | **Gender:** Male | **Coupon/UID:** NA / AOM0306

Diagnosis: Colorectal Neoplasms

MEDGENOME

MGM527: Microsatellite Instability (MSI) by fragment analysis

Report Details		Specimen Information		Ordering Clinician	
Sample ID / Order ID:	9639894 / 1569213	**Specimen Site:**	Colon	**Clinician:**	Dr. Mahendra Perera
Collection Date:	25th November 2025	**Specimen Received:**	FFPE Tissue Blocks [2]	**Affiliation:**	Aegle Omics Private Limited
Date Received:	22nd December 2025	**Specimen Tested:**	YK34563L	**Serviced By:**	18718
Report Date & Time:	30th Dec 2025 12:51 PM	**Tumor Content (%):**	55	**Report Status:**	Final

Clinical Summary:

Moderately differentiated infiltrating adenocarcinoma of sigmoid colon; T4N1bM0.

Kindly note that this is the MSI report. The final NGS report including the status of SNVs & Indels, Fusions, and CNVs, will be released on or before 08-01-2026 based on the QC status.

TEST RESULT SUMMARY

Microsatellite Instability (MSI) Status - Stable

Summary of Markers	
Count of markers reported Unstable	0
Count of markers reported Stable	12
Reported Unstable Rate	0.00%
Unstable Markers	None

CLINICAL SIGNIFICANCE

- MSI screening has long been recognized as important in the care of patients with colorectal cancer (CRC) or endometrial cancer (EC).
- High-frequency MSI (MSI-H) is also recognized as a potential marker for germline mutations in certain DNA mismatch repair (MMR) genes associated with Lynch syndrome [PMID: 15872200].
- MSI has been found in several cancer types, including non-small cell lung cancer, melanoma, breast cancer, urothelial cancer, pancreatic ductal adenocarcinoma and brain cancer. The expansion of MSI clinical trials into other cancers may elucidate the prognostic and predictive value of MSI for non-colorectal [PMID: 35955855].
- NCCN® guidelines recommend universal screening for 15+ different cancer types by MSI and/or IHC analysis [www.nccn.org]
- MSI-H status is predictive of a positive response to immunotherapies such as immune checkpoint blockade inhibitors [PMID: 26028255]
- The 2015 paper by Le et al. reported the extended analysis on the efficacy of PD-1 blockade in patients with advanced mismatch repair-deficient cancers of both colorectal cancer and non-colorectal origins. Following 41 patients, the study found that patients with mismatch repair deficient tumors, experienced an objective response rate of 40% and a progression-free survival rate of 78%. In contrast, the objective response rate was 0% and the progression-free survival rate was 11% for mismatch repair-proficient

- The College of American Pathologists (CAP),in collaboration with the Association of Molecular Pathology (AMP),American Society of Clinical Oncology (ASCO), and patient advocacy group Fight Colorectal Cancer (Fight CRC) convened a multidisciplinary expert and advisory panel to develop evidence-based guidelines to identify the optimal clinical laboratory test to identify defects in DNA mismatch repair (dMMR) in patients with solid tumor malignancies who are being considered for immune checkpoint inhibitor (ICI) therapy. MSI by PCR was recommended for colorectal cancer, patients with gastroesophageal and small bowel cancer and other solid malignancies [PMID: 35920830].
- On June 29, 2020, the Food and Drug Administration approved pembrolizumab (KEYTRUDA, Merck & Co.) for the first-line treatment of patients with unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) colorectal cancer [www.fda.gov].
- The FDA approved pembrolizumab on May 23, 2017, for the treatment of adult and pediatric patients with unresectable or metastatic, microsatellite instability-high (MSI-H), or mismatch repair deficient (dMMR) solid tumors that have progressed following prior treatment and who have no satisfactory alternative treatment options and for the treatment of unresectable or metastatic MSI-H or dMMR colorectal cancer that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan [www.fda.gov].

DISCLAIMER

- **Decisions regarding treatment action plan should not be solely based on these test results. These findings are highly recommended to be correlated with the patient's clinical, pathological, radiological and family history for decisions on diagnosis, prognosis, or therapeutics.**
- The therapy information provided in this report is based onFDA approved drugs data, NCCN guidelines, peer-reviewed published literature, standard clinical databases, and strength of biomarker results. These therapies may or may not be suitable/beneficial to a particular patient. This clinical report summarizes potentially effective medications, potentially ineffective medications, and medications that may pose a higher risk of adverse reactions by mapping the patient's genetic alterations to the biomedical reference information. The report may also provide prognostic and diagnostic biomarkers detected or shown for the given disease context.
- The identification of a genomic biomarker does not necessarily imply pharmacological effectiveness or ineffectiveness. The medications identified by the treating physician may or may not be suitable for use on a particular patient. Thus, the clinical report does not guarantee that any particular agent will be effective in the treatment of any particular condition. Also, the absence of a treatment option does not determine the effectiveness or predict an ineffective or safety-relevant effect of a medication selected by the treating physician.
- Due to poor quality of FFPE tissue blocks, the QC parameters for extracted DNA may not pass to proceed further with the testing, therefore there is a possibility of assay failure or compromised. However, sample status in such scenarios shall be sent through mail to the ordering clinician.
- This test has been validated at MedGenome Labs as per the CAP guidelines with 100% sensitivity and specificity.
- The results of this test are dependent on the tumor content in the tissue sample provided. A minimum of >10% tumour content is required for a successful testing.
- In case of MSI negative or MSS patients, if there is a co-existing strong personal or family history of HNPCC related cancers for this patient, consider microsatellite instability and IHC testing on a different tumor block to further evaluate the possible role of defective DNA mismatch repair.
- **Additional case specific disclaimer: In this case, the marker "BAT-40" had failed in amplification. Hence, the MSI status of this subject has been interpreted based on the status of 12 out of 13 markers. Kindly correlate clinically.**

TEST METHODOLOGY

This assay detects the presence of microsatellite instability (MSI) in DNA samples through multiplex PCR [1] and fragment analysis and screens for 13 mononucleotide markers listed in table below. Mononucleotide markers like BAT-25, BAT-26 and BAT-40 markers are selected as per the NCI guidelines. A revised guidelines suggests mononucleotide marker panel is more sensitive for MSI-H tumors than other microsatellite markers. Dinucleotide markers are less sensitive, and if only dinucleotide markers are positive, it is mandatory to test additional mononucleotide markers to rule out MSI-L [PMID: 14970275].This kit contains 13 mononucleotide markers for higher resolution and two STR sequences that can be used to

track sample identity [PMID: 35884597][PMID: 35982978].

ABI-16	ABI-19	ABI-20B	BAT-26	CAT-25	NR-22	NR-27
ABI-17	ABI-20A	BAT-25	BAT-40	NR-21	NR-24	

The primers are fluorophore tagged at the 5' end and the end-point PCR product is analyzed by Fluorophore Capillary Electrophoresis. The tumor tissue is classified as MSS/MSI-L/MSI-H as mentioned in the table below.

MSI Result	**Interpretation**[PMID: 35884597]
MSI-High	Unstable marker rate:- 30% - 100%
MSI-Low	Unstable marker rate:- 5% - 29.99%
MSS(Microsatellite Stable)	Unstable marker rate:- 0%

RECOMMENDATION

Test results should be interpreted in context of clinical findings, family history, and other laboratory data. If results obtained do not match other clinical or laboratory findings, please contact the laboratory for possible interpretation. Misinterpretation of results may occur if the information provided is inaccurate or incomplete.

REFERENCE

1. Application note: TrueMark MSI Assay—a simplified solution for analyzing microsatellite instability in FFPE tumor samples, 2020.

Dr Syed Muqlisur Rehman, MD
Molecular Pathologist
KMC Registration No. 71468

END OF REPORT