MAYO CLINIC LABORATORIES

1-800-533-1710

TMSI

Microsatellite Instability, Tumor

Patient ID	Patient Name		Birth Date	Gender	Age
SA00140251	TESTINGTSMI, ABNORMAL		1970-11-11	M	50
Order Number	**Client Order Number**	**Ordering Physician**	**Report Notes**		
SA00140251	SA00140251	CLIENT,CLIENT			
Account Information		**Collected**			
C7028846 DLMP Rochester		11 Nov 2020 00:00			

Tumor, Microsatellite Instability

Result Summary

MCR

MSI-H

Result

MCR

Provided diagnosis: colorectal adenocarcinoma

MSI Result: MSI-H (instability observed in 7 of 7 informative markers)

Interpretation

1 MCR

High levels of microsatellite instability (MSI-H) are indicative of defective DNA mismatch repair function within the tumor. The molecular etiology of tumors demonstrating defective DNA mismatch repair is very heterogeneous and can be associated with several different genes (MLH1, MSH2, MSH6, PMS2) and different mechanisms of gene inactivation (epigenetic, somatic, and germline alteration). The majority of sporadic colon cancers with defective DNA mismatch repair (approximately 90%) are caused by somatic epigenetic alterations, specifically hypermethylation of the MLH1 promoter.

THERAPEUTIC IMPLICATIONS

Current data suggest that advanced stage solid tumors with defective DNA mismatch repair (MSI-H) are more likely to respond to treatment with immunotherapies such as anti-PD-1 therapies (Science. 2017 Jul 28;357(6349):409–413(PMID 28596308); J Clin Oncol. 2018 Jan 20:JCO2017769901 (PMID 29355075)). Stage II patients with colon cancers characterized by the presence of defective DNA mismatch repair (MSI-H) are unlikely to derive benefit from treatment with 5-FU based therapy (J Clin Oncol. 2010 Jul 10;28(20):3219–26 (PMID 20498393)).

HEREDITARY IMPLICATIONS

These results increase the risk that this individual has HNPCC/Lynch syndrome because tumors exhibiting an MSI-H phenotype can be associated with a germline mutation in one of the DNA mismatch repair genes. The use of immunohistochemistry (IHC / MMR Protein, IHC Only, tumor), followed by germline mutational analysis, can further evaluate the possibility of HNPCC/Lynch syndrome in this individual. A genetic consult may be of benefit.

PROGNOSTIC IMPLICATIONS

Colon cancers with defective DNA mismatch repair (MSI-H) have a significantly better prognosis compared to those with intact mismatch repair (MSS) (J Clin Oncol. 2005 Jan 20;23(3):609–18 (PMID 15659508)).

ADDITIONAL INFORMATION

Consideration of these results, in light of other clinical information, may aid in clinical management decisions for this patient.

Of note, the literature suggests that MSI analysis on neoadjuvant chemoradiated tumor specimens may influence MSI status and lead to an erroneous interpretation of results (Int J Radiat Oncol Biol Phys. 2007 68(5):1584).

These data should be interpreted in the context of the histopathologic findings. A surgical pathology consult may be ordered separately. If immunohistochemistry (IHC) for the mismatch repair proteins was also ordered on this specimen, the results will be reported separately under test code IHC (IHC / MMR Protein, IHC Only, Tumor). For questions regarding the interpretation of IHC and MSI results, please contact the Genomics Laboratory at 1–800–533–1710.

ADDITIONAL INFORMATION

Microscopic examination was performed by a pathologist to identify areas of normal and tumor for enrichment by macrodissection. A PCR-based assay is used to test for tumor microsatellite instability (TMSI) with the use of 7 mononucleotide repeat markers (ACVR2A, BTBD7, DIDO1, MRE11, RYR3, SEC31A, and SULF2). The tumor tissue is classified as MSS (instability detected in 0 or 1 out of 7 markers), or MSI-H (instability in 2 or more of 7 markers tested). Due to the sensitivity of the method being used, microsatellite instability cannot be reliably detected in colorectal samples containing less than 20% tumor DNA or samples from other tumors containing less than 40% tumor DNA. Samples are routinely macrodissected to enrich for tumor cells, with colorectal samples less than 20% and other tumor types less than 40% rejected from further testing. Test results should be interpreted in the context of clinical findings, family history, and other laboratory data. If results

Performing Site Legend

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

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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.

Specimen MCR

Tissue, Tumor

Tissue ID MCR

1234

Released By MCR

Kevin C. Halling, M.D., Ph.D.

Received: 11 Nov 2020 13:09 **Reported:** 11 Nov 2020 13:59

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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