MAYO CLINIC LABORATORIES

Test Definition: TMSI

Microsatellite Instability, Tumor

Overview

Useful For

Evaluation of tumor tissue to identify patients at high risk for having Lynch syndrome, also known as hereditary nonpolyposis colorectal cancer

Evaluation of tumor tissue for clinical decision-making purposes given the prognostic and therapeutic implications associated with microsatellite instability phenotypes

Additional Tests

Test Id	Reporting Name	Available Separately	Always Performed
SLIRV	Slide Review in MG	No, (Bill only)	Yes

Testing Algorithm

When this test is ordered, slide review will always be performed at an additional charge.

For more information see Lynch Syndrome Testing Algorithm

Special Instructions

- Molecular Genetics: Inherited Cancer Syndromes Patient Information
- Lynch Syndrome Testing Algorithm

Method Name

Polymerase Chain Reaction (PCR)

NY State Available

Yes

Specimen

Specimen Type

Varies

Necessary Information

1. A pathology report (final or preliminary) is required and must accompany specimen for testing to be performed.

2. The following information must be included in the report provided.

-Patient name

-Block number-**must be on all blocks, slides and paperwork** (can be handwritten on the paperwork)

-Date of tissue collection

-Source of the tissue

Specimen Required

This assay requires at least 40% tumor nuclei for endometrial specimens and at least 20% tumor nuclei for colorectal specimens.

-Preferred amount of tumor area with sufficient percent tumor nuclei: tissue 72 mm(2)
-Minimum amount of tumor area: 18 mm(2)
-These amounts are cumulative over up to 10 unstained slides and must have adequate percent tumor nuclei.
-Tissue fixation: formalin-fixed paraffin-embedded, non-decalcified

Preferred:
Specimen Type: Tissue block
Collection Instructions: Submit a formalin-fixed, paraffin-embedded tissue block with acceptable amount of tumor tissue.

Acceptable:
Specimen Type: Tissue slide
Slides: 1 Hematoxylin and eosin stained and 5 unstained
Collection Instructions: Submit 1 slide stained with hematoxylin and eosin and 5 unstained, nonbaked slides with 5-micron thick sections of the tumor tissue.
Note: The total amount of required tumor nuclei can be obtained by scraping up to 5 slides from the same block.

Forms

1. Molecular Genetics: Inherited Cancer Syndromes Patient Information (T519)
2. If not ordering electronically, complete, print, and send 1 of the following forms with the specimen:
-Gastroenterology and Hepatology Test Request (T728)
-Oncology Test Request (T729)

Specimen Minimum Volume

See Specimen Required

Reject Due To

Specimens that have been decalcified (all methods) Specimens that have not been formalin-fixed, paraffin-embedded Bone marrow in EDTA	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Ambient (preferred)		
	Refrigerated		
	Frozen		

Clinical & Interpretive

Clinical Information

Somatic (tumor-specific) microsatellite instability (MSI) is assessed by this test. MSI is characterized by numerous alterations in a type of repetitive DNA called microsatellites and occurs as the result of an impaired DNA mismatch repair process. Impaired DNA mismatch repair is a key factor in tumorigenesis and can occur sporadically or as the result of a hereditary cancer predisposition called Lynch syndrome.

Evaluation for MSI may be valuable for clinical decision making. Current data suggest that advanced stage solid tumors with defective DNA mismatch repair (MSI-high: MSI-H) are more likely to respond to treatment with immunotherapies, such as anti-PD-1 therapies. Colon cancers that demonstrate defective DNA mismatch repair (MSI-H) have a significantly better prognosis compared to those with intact mismatch repair (microsatellite stable/MSI- low: MSS/MSI-L). Additionally, current data indicate that stage II and stage III patients with colon cancers characterized by the presence of defective mismatch repair (MSI-H) may not benefit from treatment with fluorouracil alone or in combination with leucovorin. These findings are most likely to impact the management of patients with stage II disease.

MSI analysis, usually in combination with immunohistochemistry staining of the mismatch repair proteins, can also provide helpful diagnostic information in the context of evaluation for Lynch syndrome. See Lynch Syndrome Testing Algorithm.

Reference Values

An interpretive report will be provided.

Interpretation

The report will include specimen information, assay information, and interpretation of test results.

Microsatellite stable (MSS) is reported as MSS (0 or 1 of 7 markers demonstrating instability) or microsatellite instability-high (MSI-H) (2 or more of 7 markers demonstrating instability).

Cautions

The finding of tumor microsatellite instability does not distinguish between somatic and germline alterations.

Test results should be interpreted in the context of clinical findings, family history, and other laboratory data. Errors in the interpretation of results may occur if requested information is inaccurate or incomplete.

Supportive Data

A total of 100 accuracy samples were run retrospectively during verification; 55/100 samples were colorectal, 41/100 were endometrial, and the remaining 4/100 were other tumor types. The overall concordance between the Idylla and Promega results was 98/100 (98%). Seventy-nine of 100 samples were microsatellite stable (MSS) by Promega and 77 (97%) had concordant MSS results by Idylla. Twenty-one of 100 samples were microsatellite instability-high (MSI-H) by

Promega and 21 (100%) had concordant MSI-H results by Idylla.

In addition to the retrospective samples, 100 consecutive samples were prospectively analyzed, of which 58 were colorectal, 31 were endometrial, and 11 were from other tumor types. Seventy-six of 100 samples were MSS by Promega and all (100%) were MSS by the Idylla assay. Twenty-four of 100 samples were MSI-H by Promega. Twenty-three of 24 (96%) of the MSI-H samples were concordant by Idylla. One patient had an uncommon reason for testing. The discordant sample DNA was rerun on the Promega platform, but there was not sufficient tissue remaining to rerun this specimen on the Idylla assay. After reviewing the results from the 2 runs on Promega, a consensus decision amongst 5 pathologists was reached, and the sample was reclassified as equivocal by the Promega assay.

Precision and reproducibility were evaluated by running 3 MSI-H samples and 3 MSS samples in triplicate on the same instrument. Each of these samples had a 4th cartridge run on a separate instrument. There was 100% concordance between replicates from the 3 MSI-H samples and 3 MSS samples.

Clinical Reference

1. Baudhuin LM, Burgart LJ, Leontovich O, Thibodeau SN. Use of microsatellite instability and immunohistochemistry testing for the identification of individuals at risk for Lynch syndrome. Fam Cancer. 2005;4(3):255-265
2. Terdiman JP, Gum JR Jr, Conrad PG, et al. Efficient detection of hereditary nonpolyposis colorectal cancer gene carriers by screening for tumor microsatellite instability before germline genetic testing. Gastroenterology. 2001;120(1):21-30
3. Popat S, Hubner R, Houlston RS. Systematic review of microsatellite instability and colorectal cancer prognosis. J Clin Oncol. 2005;23(3):609-618
4. Ribic CM, Sargent DJ, Moore MJ, et al. Tumor microsatellite-instability status as a predictor of benefit from fluorouracil-based adjuvant chemotherapy for colon cancer. N Engl J Med. 2003;349(3):247-257
5. Idos G, Valle L. Lynch syndrome. In: Adam MP, Mirzaa GM, Pagon RA, et al, eds. GeneReviews [Internet]. University of Washington, Seattle; 2004. Updated February 4, 2021. Accessed July 30, 2024. Available at www.ncbi.nlm.nih.gov/books/NBK1211/
6. Kawakami H, Zaanan A, Sinicrope FA. Microsatellite instability testing and its role in the management of colorectal cancer. Curr Treat Options Oncol. 2015;16(7):30
7. Sargent DJ, Marsoni S, Monges G, et al. Defective mismatch repair as a predictive marker for lack of efficacy of fluorouracil-based adjuvant therapy in colon cancer. J Clin Oncol. 2010;28(20):3219-3226
8. Le DT, Durham JN, Smith KN, et al. Mismatch repair deficiency predicts response of solid tumors to PD-1 blockade. Science. 2017;357(6349):409-413
9. Overman MJ, Lonardi S, Wong KYM, et al. Durable clinical benefit with nivolumab plus ipilimumab in DNA mismatch repair-deficient/microsatellite instability-high metastatic colorectal cancer. J Clin Oncol. 2018;36(8):773-779

Performance

Method Description

The Idylla is a fully automated real-time polymerase chain reaction based molecular testing system that uses formalin-fixed, paraffin-embedded slides. This assay detects a novel panel of 7 monomorphic biomarkers (ACVR2A, BTBD7, DIDO1, MRE11, RYR3, SEC31A, SULF2) to evaluate microsatellite instability status without need for normal (noncancerous) tissue from each patient.(Unpublished Mayo method)

PDF Report
No

Day(s) Performed
Varies

Report Available
4 to 7 days

Specimen Retention Time
FFPE tissue: Unused portions of FFPE blocks will be returned. Unused, unstained slides: 5 years; Stained slides: Indefinitely.

Performing Laboratory Location
Rochester

Fees & Codes

Fees
- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification
This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information
81301
88381-Microdissection, manual

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
TMSI	Tumor, Microsatellite Instability	81711-4

Result ID	Test Result Name	Result LOINC® Value
609365	Result Summary	50397-9
609366	Result	43368-0
609367	Interpretation	69047-9
609368	Specimen	31208-2
609369	Source	31208-2
609370	Tissue ID	80398-1
609371	Released By	18771-6