



Microsatellite Instability (MSI)

FDA-approved tumor-agnostic predictive biomarker for Immunotherapy



- Microsatellite instability (MSI/MSI-H) are regions of short repeated DNA (1-9 nucleotides).
- Accumulation of mutations (insertions or deletions of a few nucleotides) in microsatellites is caused by deficient DNA mismatch repair system (MMR) and leads to microsatellite instability (MSI).
- MMR system comprises at least ten proteins including MLH1, MSH2, MSH6, and PMS2, which are the most frequently mutated or epimutated (MLH1) genes in cancer.



MSI Testing Methodology



Clinical Implications of MSI Test

MSI as a Biomarker for Hereditary Cancer Risk:

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- Clinically important to screen in all solid cancers especially in colorectal cancer and endometrial cancer
- Potential marker for germline mutations in Mismatch repair (MMR) genes associated with Lynch Syndrome

MSI as a Biomarker for Response to Immunotherapy:

 In solid tumours, defective MMR (dMMR) pathway results in multiple mutated proteins which may elicit immunogenic responses \cap

• These tumours are found to be susceptible to immune checkpoint inhibitors (Immunotherapy)

The FDA has granted full approval to pembrolizumab for the treatment of adult and pediatric patients with unresectable or metastatic microsatellite instability-high or mismatch repair-deficient solid tumors that have progressed following previous treatment and who have no satisfactory alternative options.

Reference: https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-pembrolizumab-first-tissuesite-agnostic-indication

CAP and ASCO 2023 Recommendations: MSI Testing for Immunotherapy

Cancer Type	Testing Recommendation	MedGenome Offerings	
Colorectal cancer	 dMMR by IHC and/or MSI by PCR Validated MSI by NGS against dMMR by IHC or MSI by PCR 	dMMR by IHC	
Gastroesophageal and small bowel cancer (Does not include Esophageal squamous cell carcinoma)	• dMMR by IHC and /or MSI by PCR	MSI by PCR (13 markers)	
Endometrial cancer	• dMMR by IHC		
Other cancer types than mentioned above	• Not established; validated assay for a specific tumor type has been conditionally recommended	MSI by NGS (27 markers)	

Test Details

Test Code	Test Name	Specimen Type	Methodology	ТАТ
MGM312	Lynch Syndrome Mismatch Repair (MMR) by IHC [MLH1, MLH2, MSH6 & PMS2]		Protein expression analysis by Immunohistochemistry (IHC)	4 Working days
MGM527	Microsatellite Instability (MSI) by Fragment Analysis	FFPE tissue block	Fragment analysis by PCR (13 markers)	7 Working days
MGM2685	Microsatellite Instability (MSI) by NGS		Next generation sequencing (27 markers)	14 Working days