

## Microsatellite Instability (MSI): New Molecular Diagnostics Test

Date: December 22, 2020

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Effective Date: January 20, 2020

The Molecular Diagnostics laboratory will offer PCR-based Microsatellite Instability (MSI) testing. MSI testing is used to identify tumors with defective mismatch repair (MMR). Since insertion/deletion errors occur frequently during replication of repetitive DNA sequences, MMR-deficient tumors are prone to accumulating insertion/deletion errors in microsatellites. PCR-based MSI testing works by assessing the number of nucleotide repeats in a defined panel of microsatellites in a block of tumor and comparing the number of repeats to a block of non-tumor tissue from the same individual. The test complements MMR testing by IHC, and can identify the occasional MSI-High (MSI-H) tumor that shows retained nuclear expression of all four MMR genes by IHC.

Identification of MMR-deficient tumors is important for two reasons:

1. MSI-H/MMR-deficient tumors are more likely to show durable response to anti-PD-1/PD-L1 therapy.
2. MSI-H/MMR-deficient tumors can arise in the setting of Lynch Syndrome. In some contexts, patients with MSI-H/MMR-deficient tumors may be referred for genetic counseling and consideration for germline testing, with implications for management of family members.

Pathologists should request PCR-based MSI testing in the following settings:

1. MMR IHC shows equivocal/questionable results.
2. There is suspicion of a familial cancer syndrome but retained expression of MMR genes by IHC.
3. If specifically requested by a clinical colleague. (Note: 'MSI testing' refers to MMR IHC and consideration of reflex PCR-based testing as above.)

When selecting tumor block, any well-preserved viable tumor with greater than 25% cellularity should be adequate. When selecting control tissue, any benign block with decent viable cellularity will suffice, but tumor-draining lymph nodes are to be avoided.

Resulting will be provided, as follows:

1. MSI-High: 2 or more of the 5 markers is altered
2. MSI-Low (MSI-L): 1 of 5 markers is altered; or MSS (microsatellite stable): All 5 markers are unaltered.

(For clinical purposes, only MSI-H is actionable).



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To request this assay, the molecular laboratory will need the following information. An example of how it might be completed is below:

### ANCILLARY STUDIES

Case	20-HSP99999
Name	
Tumor Block	A3, A10
Control Block (required)	A1
Special stains	
IHC	
Molecular	MSI testing
Cytogenetics	
Indication (tumor type)	Multifocal CRC with suspected Lynch but intact MMR by IHC

### MOLECULAR REQUESTS ALSO FILL OUT FORM BELOW:

<b>Additional Copies to Doctors:</b>	[your name], [oncologist] , [include Carol Lustig, NP-if testing due to suspicion of Lynch syndrome],
Tumor is dispersed throughout with >25% tumor cells. (If yes, histo to send curls, no H&E required)	[No] [Yes] (% tumor cellularity in total tissue)]
Tumor is clustered with significant non-neoplastic background tissue Histology to prepare H&E and unstains, and pathologist is to circle area enriched in tumor on HE slide.	[No] [Yes % (tumor cellularity in circled area)]
Organ (lung, lymph node, pleural, colon, etc):	Colon

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