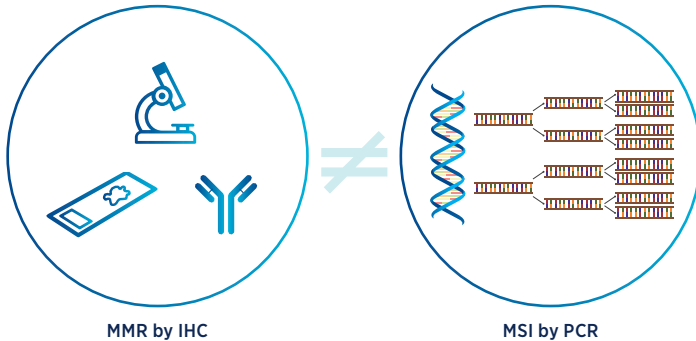


MSI TESTING MOLECULAR PCR VERSUS TRADITIONAL IHC TESTING



TRADITIONAL IHC TESTING VERSUS MOLECULAR PCR TESTING



MSI by PCR and deficient MMR by IHC provide fundamentally different information about tumor samples.

Immunohistochemistry (IHC) measures the presence or absence of Mismatch Repair (MMR) proteins; however, the presence of MMR protein expression is not necessarily a conclusive measure of MMR function. There can be a loss in function of these proteins without a corresponding loss of the protein in the cell, with 5-10% of proteins retaining antigenicity when they are not functional.¹

Microsatellite Instability (MSI) by PCR directly measures changes in DNA caused by loss of MMR protein function as opposed to assessing the proteins themselves in IHC.

This makes MSI a functional measure of mismatch repair deficiency that detects loss in MMR repair function, regardless of the cause.¹

MSI TESTING IS RECOMMENDED FOR VARIOUS APPLICATIONS

MSI TESTING FOR LYNCH SCREENING

In international guidelines **both MMR by IHC and/or MSI by PCR are recommended** methods for Lynch screening.²

The **decision** about which screening method to be used depends primarily on the **availability of resources** and **expertise of the lab**.

ESMO RECOMMENDATION FOR CO-TESTING IN METASTATIC COLORECTAL CANCER FOR IMMUNOTHERAPY INDICATION

ESMO recommends to combine both tests to assess the eligibility to treatment with immune checkpoint inhibitors of mCRC and other cancers of the Lynch syndrome spectrum.^{3,4}

IHC LACKS STANDARDIZATION WITH POTENTIAL IMPACT ON PERFORMANCE

CURRENT IHC CHALLENGES – RESULT REPORTING

- Subjective interpretation
- Molecular confirmation needed for doubtful cases
- No consensus criteria on staining cut-off⁵
- Missense mutations in MMR genes leading to false negative result interpretation

CURRENT IHC CHALLENGES – WORKFLOW

- Wide variability of antibodies⁶

Proportion of sufficient results for MSH6 in NordiQC runs performed

	Run 32 2011	Run 43 2015	Run 52 2018
Participants, n=	90	153	242
Sufficient results	33%	63%	52%

- The recommendation to use 4 MMR antibodies is not yet widely adopted
- Wide variation in protocol parameters (e.g. dilution and incubation times)

IDYLLA™ MSI TEST ENSURES OPTIMAL DIAGNOSTIC RESULTS

Standardized, fully automated Idylla™ MSI testing overcomes the barriers of traditional PCR and IHC testing.



Features/Benefits	IHC	Traditional PCR	Idylla™ MSI
Identification of defective protein	✓	-	-
Consequence of inactivation	-	✓	✓
Results within 2,5 hours	✓	-	✓
Limited hands-on time	-	-	✓
No batching needed	✓	-	✓
MSI testing in any laboratory setting	✓	-	✓
Standardized	-	-	✓
CE IVD from tissue to result	-	-	✓
Moving towards IVDR compliance	-	-	✓
Only 1 FFPE tissue section needed	-	-	✓
No need for paired normal tissue sample	-	-	✓
Fully automated sample-to-result	-	-	✓
Contamination control	-	-	✓
Objective result interpretation	-	-	✓



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