

MSI TESTING IHC STAINING VERSUS MOLECULAR PCR TESTING



THINK IDYLLA™
BECAUSE TIME MATTERS

IDYLLA™ CDx MSI TEST ENSURES OPTIMAL DIAGNOSTIC RESULTS

The standardized, fully automated Idylla™ CDx MSI Test overcomes the barriers of traditional PCR and IHC testing.

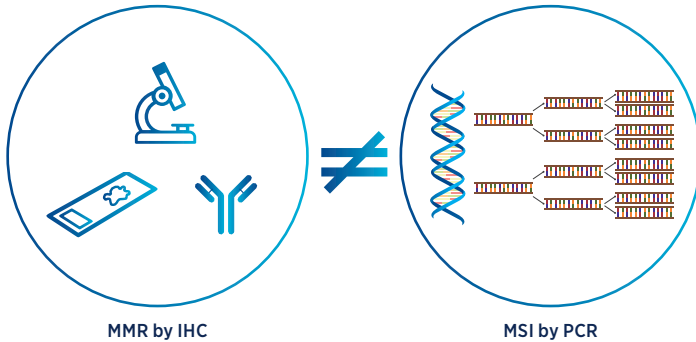
Features	IHC	Traditional PCR*	Idylla™ CDx MSI
Identification of defective protein	✓	-	-
Detection of genomic instability	-	✓	✓
Results within 2.5 hours	✓	-	✓
Limited hands-on time	-	-	✓
No batching needed	✓	-	✓
MSI testing in any laboratory setting	✓	-	✓
Standardized	-	-	✓
IVD from tissue to result	-	-	✓
IVDR-compliant (CDx)	✓	-	✓
Only 1 FFPE tissue section needed**	-	-	✓
No need for paired normal tissue sample	✓	-	✓
No need for external controls	-	-	✓
Fully automated sample-to-result	-	-	✓
Contamination control	-	-	✓
Objective result interpretation	-	-	✓

*PCR-based fragment-sizing test

**≥ 33% neoplastic cells and tissue area 25-300 mm² (10 μm)



IHC STAINING VERSUS MOLECULAR PCR TESTING



MSI testing by PCR and MMR assessment by IHC provide fundamentally different insights into tumor samples.

Immunohistochemistry (IHC) evaluates the presence or absence of mismatch repair (MMR) protein expression; however, detectable protein expression does not necessarily indicate intact MMR function. Approximately 5–10% of tumors with impaired MMR function retain MMR protein expression, potentially leading to false-negative dMMR results.

Microsatellite instability (MSI) testing by PCR detects DNA changes caused by defective mismatch repair. Unlike IHC, MSI provides a functional assessment of MMR activity, identifying deficiencies even when the proteins stain positive but are non-functional.¹

MSI TESTING IS RECOMMENDED FOR VARIOUS APPLICATIONS

GUIDELINES ON MSI TESTING FOR LYNCH

In international guidelines **both MMR by IHC and/or MSI by PCR are recommended** methods for pre-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 combining 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

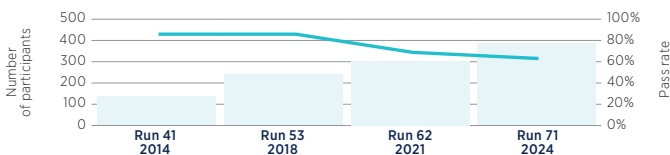
IHC REPORTING CHALLENGES

- Subjective interpretation^{5,6}
- Molecular confirmation needed for equivocal cases
- No consensus on staining cut-off⁷ criteria
- MMR gene mutations may result in impaired functional activity without absence of MMR protein staining⁸

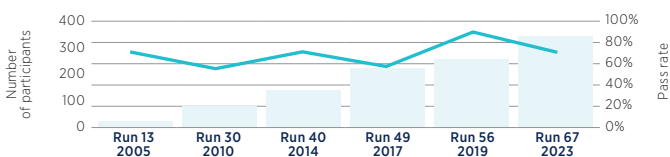
IHC WORKFLOW CHALLENGES

- Wide variability of antibody performance⁹

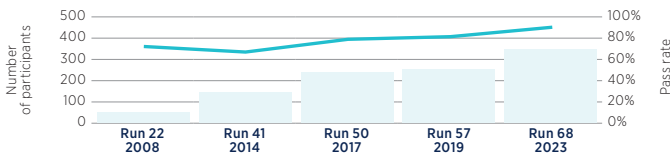
Proportion of sufficient results for PMS2 in the four NordiQC runs performed¹⁰



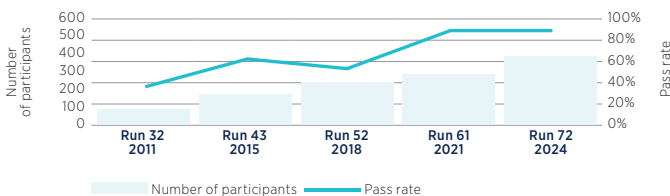
Proportion of sufficient results for MLH1 in the six NordiQC runs performed¹¹



Proportion of sufficient results for MSH2 in the five NordiQC runs performed¹²



Proportion of sufficient results for MSH6 in the five NordiQC runs performed¹³



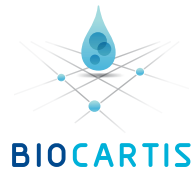
- The recommendation to use four MMR antibodies is not yet widely adopted
- Wide variation in protocol parameters (e.g., antibody dilution and incubation times)
- The use of less sensitive detection systems¹²

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- (10) NordiQC Assessment Run 71 2024 - Mismatch Repair Protein PMS2 (PMS2): https://www.nordiqc.org/downloads/assessments/188_84.pdf
- (11) NordiQC Assessment Run 67 2023 - Mismatch Repair Protein MLH1 (MLH1): https://www.nordiqc.org/downloads/assessments/171_81.pdf
- (12) NordiQC Assessment Run 68 2023 - Mismatch Repair Protein MSH2 (MSH2): https://www.nordiqc.org/downloads/assessments/172_82.pdf
- (13) NordiQC Assessment Run 72 2024 - Mismatch Repair Protein MSH6 (MSH6): https://www.nordiqc.org/downloads/assessments/189_83.pdf

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