Modaplex MSI

MICROSATELLITE INSTABILITY TESTING

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BIOTYPE

MSI IN CLINICAL RESEARCH

FROM PROMISING CANDIDATE TO CLINICAL PRACTICE

MSI AS RESEARCH MARKER FOR IMMUNE-CHECKPOINT THERAPY RESPONSE

In recent years, immune-checkpoint inhibitors (ICIs) have revolutionized the treatment of patients with advanced cancer and ICIs have become a strong pillar in cancer treatment[1]. However, understanding the molecular biological background is still required when considering the best indication for ICI[2]. In this context several studies have demonstrated that MSI status, as a surrogate for a defective mismatch repair system (dMMR), is a positive predictor for the response to immune-checkpoint inhibitors[3,4,5]. Furthermore, since 2017 several IC-therapies have been approved by the US Food and Drug Administration (FDA) or EMA considering the tumor´s MSI status.

As the MSI status is a practical marker, clinical researchers are currently investigating MSI and its implications for predicting the response to immune checkpoint blockade in a variety of tumor entities[6].

INVESTIGATION OF MSI IN ENDOMETRIAL CARCINOMA

The Cancer Genome Atlas Research Network (TCGA) performed an integrating genomic, transcriptomic and proteomic characterization of endometrial carcinoma. Exome sequence analysis revealed four groups of tumors[7].

- **Group 1** carcinomas have somatic inactivating hotspot mutations in the POLE exonuclease domain and a very high mutational burden (ultramutated).
- **Group 2** include endometrioid carcinomas with microsatellite instability (MSI) (hypermutated), frequently with MLH-1 promoter hypermethylation and high mutation rates.
- **Group 3** tumors include endometrioid carcinoma with low copy number alterations, and low mutational burden, while lacking POLE mutations and MSI-H.
- **Group 4** (Serous-like or copy-number high) show a low mutation rate, nearly universal TP53 mutations, and a highly unfavorable prognosis.

Clinical researchers are now attempting to bring the TCGA molecular-based classification into clinical practice[8].

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INTRODUCING THE MODAPLEX MSI SOLUTION

DETERMINE MSI-H WITH MODAPLEX MSI ANALYSIS KIT

GET ACCESS TO STANDARDIZED AND INDIVIDUAL MSI-H ASSESSMENT

- Simultaneous analysis of proven dinucleotide and mononucleotide markers
- Individually determine MSI-H status according to standardized assessment options
- Facilitate decision making through intuitive result analysis

REPORT RESULTS WITH CONFIDENCE

- Verified with artificial material and tested on FFPE-derived CRC and EC sample material
- Include forensically accepted (human insertion/deletion polymorphism) marker as sample mix-up and contamination control
- Comprehensible MSI-H detection using optimal 10ng genomic DNA

ENHANCE LABORATORY EFFICIENCY

- Efficient workflow through automation
- Intuitive result interpretation with Biotype´s Modaplex Result Analyzer (Moda-RA) software
- Accelerate decision making with simultaneous testing on MSI- and POLE Mutation status

MODAPLEX MSI ANALYSIS KIT

PROVEN MARKER TO EMPOWER STANDARDIZED MSI-H ASSESSMENT

The combination of five mononucleotide markers (Bat-25, Bat-26, NR-21, NR-24, and Mono-27) and two dinucleotide markers (D5S346 and D17S250) allows the individual MSI analysis according to standardized assessment options. Established and developed to evaluate MSI status in colorectal cancer, this microsatellite panel have been proven to be highly sensitive and specific in providing results on MSI status across various tumor entities, such as endometrial carcinoma[1,2].

CHOOSE YOUR INDIVIDUAL STANDARDIZED MSI-H ASSESSMENT OPTION

Mononucleotide Markers	» Bat-25 » Bat-26 » NR-21 » NR-24 » Mono-27
Dinucleotide Markers	» D5S346 » D17S250

MSI assessment using mononucleotide- and dinucleotide-repeat marker[3]

	> 5 Microsatellite Markers	Interpretation
No. of marker exhibiting instability	≥ 30-40%	**MSI-H**
	< 30-40%	**MSI-L**
	0	**MSS**

Mononucleotide Markers	» Bat-25 » Bat-26 » NR-21 » NR-24 » Mono-27

MSI assessment using five quasi-monomorphic mononucleotide-repeat marker[4]

	5 Mononucleotide Markers	Interpretation
No. of marker exhibiting instability	≥ 3	**MSI-H**
	≤ 2	**MSI-L**
	0	**MSS**

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2 Siemanowski, Janna et al. "Managing Difficulties of Microsatellite Instability Testing in Endometrial Cancer-Limitations and Advantages of Four Different PCR-Based Approaches." Cancers vol. 13,6 1268. 12 Mar. 2021

3 C.R. Boland et al. "A National Cancer Institute Workshop on Microsatellite Instability for cancer detection and familial predisposition: development of international criteria for the determination of microsatellite instability in colorectal cancer." Cancer research vol. 58,22 (1998): 5248-57.

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EVALUATION OF INSTABILITY

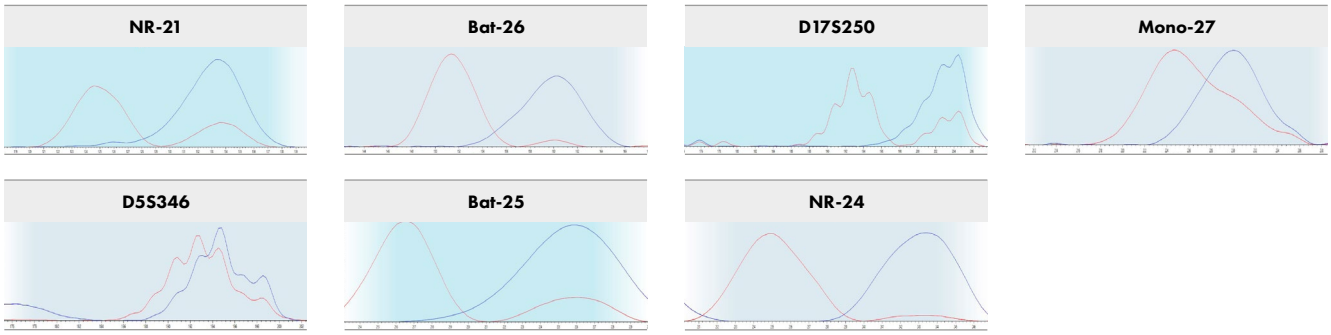
EXPERIENCE INTUITIVE ASSESSMENT THROUGH AUTOMATIC PEAK-OVERLAY

Recently, certain testing procedures are available to determine the accurate MSI-H status such as PCR-based-, NGS-based- or fully automated approaches. Interestingly, several studies have demonstrated that different methods produce concordant results 95% - 100% when compared to each other[1,2,3].

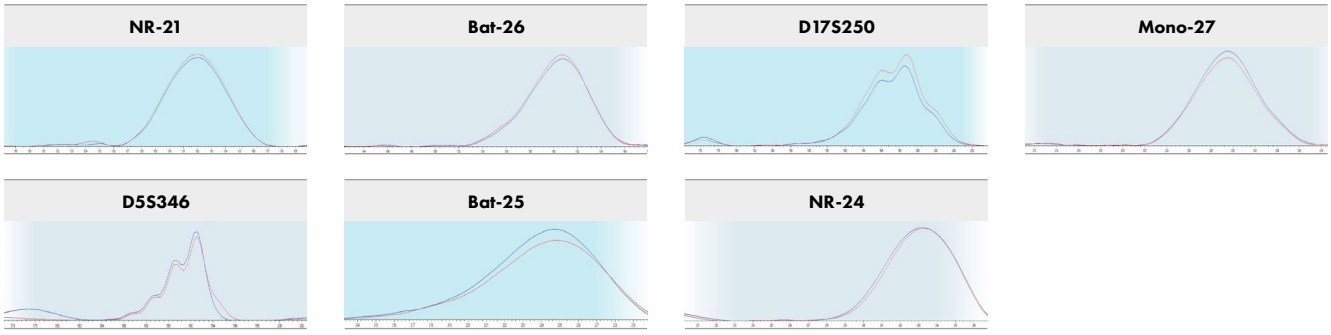
Regardless of the method, instability assessment requires careful estimation and knowledge of the technical limitations. For PCR-based systems, experience means to be knowledgeable on peak alterations and shift events. With Modaplex Result Analyzer Software, users can evaluate these peak alterations and shift events intuitively through an automated overlay of allele-peaks from tumoral and normal tissue.

INTUITIVE ASSESSMENT TO EVALUATE THE "INSTABILITY" OF EACH MARKER

Typical results from a MSI-H FFPE colorectal cancer sample, 10ng; cancer tissue (red); normal adjacent tissue (blue)



Typical results from a MSS FFPE colorectal cancer sample, 10ng; cancer tissue (red); normal adjacent tissue (blue)



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3 J. Siemanowski et al. "Managing Difficulties of Microsatellite Instability Testing in Endometrial Cancer-Limitations and Advantages of Four Different PCR-Based Approaches." Cancers vol. 13,6 1268. 12 Mar. 2021

MODAPLEX MSI ANALYSIS KIT FEATURES

REPORT RESULTS WITH CONFIDENCE

Modaplex MSI Analysis Kits provide users trustworthy MSI results. For this purpose, the kit is designed and developed according to customer requirements, ensuring a robust, safe, and flexible assay.

TAILORED TO LABORATORY REQUIREMENTS

To address the limitations of poor quantity and quality of DNA in a formalin-fixed, paraffin-embedded environment, the Modaplex MSI assay has been verified on CRC and EC FFPE samples.

RELIABLE RESULTS

The MSI assay is endowed with a comprehensive control concept. It comprises internal controls like a migration size standard as well as external positive and negative controls. In addition, the assay includes a forensically accepted marker as the sample-mix up and contamination control.

APPLICABLE FOR LOW SAMPLE AMOUNTS

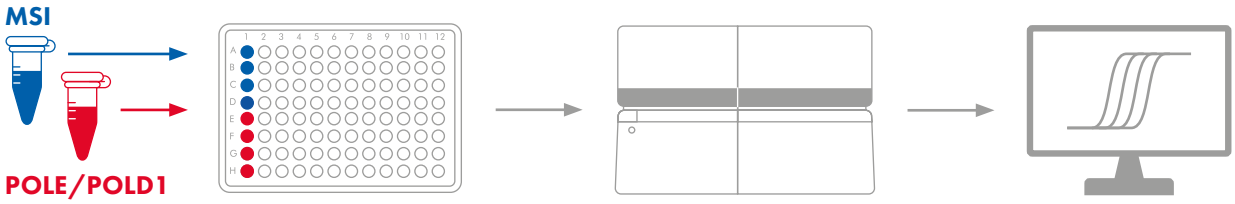
The Modaplex MSI assay is suitable for MSI-H detection using small sample inputs. Optimized to be used with a DNA input of 10ng, the assays are suitable for the widespread application on FFPE-derived sample material.

MODAPLEX MSI WORKFLOW

ENHANCE LABORATORY EFFICIENCY

The Modaplex MSI Analysis Kit is designed for use with the Modaplex instrument, a multiplex PCR bench-top system. It combines qPCR with capillary electrophoresis (CE) in an automated process and allows users to detect, differentiate, and quantify up to 50 DNA and RNA targets in a single well and run. Therefore, users can individually combine tests for the purposes of mutational analysis, gene expression, copy number variation, gene fusion, and miRNA, among many others.

STREAMLINE LABORATORY OPERATIONS WITH A COMMON PROTOCOL



PCR set up
15 min

Automated Modaplex run
~ 3 hrs

Analysis with Moda-RA
15 min

3.5 hrs

Because Modaplex assays will make use of a universal PCR program, you can perform these assays simultaneously through a workflow which is simple as setting up a PCR. Thus, microsatellite fragment analysis and POLE / POLD1 mutation detection can be individually combined and flexibly performed in a single Modaplex run in less than 3.5 hours.

ORDER INFORMATION

Product	Cat. no.	Application
Modaplex MSI Analysis Kit	85-10701-0050*	RUO
Modaplex instrument	00-04901-0001	

For research use only. Not for use in diagnostic procedures.
*Not available in Italy and the USA

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