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OncoMate™ MSI
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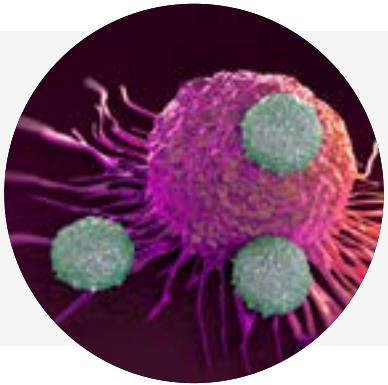
What is the OncoMate™ MSI Dx Analysis System?

The OncoMate™ MSI Dx Analysis System is a CE-Marked IVD Medical Device for the characterization of a tumor's microsatellite instability (MSI) status. The system offers physicians a functional measure of the level of DNA mismatch repair deficiency demonstrated within their patient's tumor.

The OncoMate™ MSI Dx System offers actionable results that can be used clinically as described by a multitude of global clinical guidelines to better inform potential immunotherapy decisions and assist in the diagnosis of hereditary cancer syndromes, like Lynch syndrome.

Patients with MSI-H Tumors are More Likely to Respond to Immune Checkpoint Inhibitor Therapies.

MSI high (MSI-H) tumors express protein neoantigens that can result in lymphocyte infiltration. Some tumors can block immune activation through the expression of PD-L1. This tumor induced inhibition of immune cell activity can be overcome with immune checkpoint inhibitor (ICI) therapies, which enhance the immune response against tumor cells and generally improve a patient's response to these treatments.[1–3]



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[1]Mandal, R. *et al.* (2019) Genetic diversity of tumors with mismatch repair deficiency influences anti-PD-1 immunotherapy response. *Science* **364**, 485–91.

[2]Dudley, J.C. *et al.* (2016) Microsatellite Instability as a Biomarker for PD-1 Blockade. *Clin. Cancer Res.* **22**, 813–820.

[3]Kok, M *et al.* (2019) How I treat MSI cancers with advanced disease. *ESMO Open* 4:e000511. doi:10.1136/esmoopen-2019-000511.

Better Information to Inform Better Treatment Decisions

The MSI gold standard research tool is now an IVD, enabling better access for clinical diagnostics laboratories. The OncoMate™ MSI Dx Analysis System is a CE-Marked IVD Medical Device, leveraging the same informative MSI loci relied on by global clinical researchers for almost two decades. The improved system is designed for use as a diagnostic with cancer patients to better inform testing and treatment options.

DNA from Solid Tumors All types	**~ 2.5 Hours** from DNA to answer	**≤1 FFPE** section needed	**1ng** of DNA

What is MSI?

Microsatellite Instability is the accumulation of insertion or deletion errors at microsatellite repeat sequences in cancer cells as a result of a functional deficiency within one or more major DNA mismatch repair proteins (dMMR).

Mononucleotide (homopolymer) repeat microsatellite sequences found throughout the genome are particularly sensitive to transcription errors. Thus, high frequency microsatellite instability (MSI-H) is considered a marker for the presence of mutations in, or methylation silencing of, certain major DNA MMR genes.

Watch the video to learn how MSI works

Why Order MSI Testing?

Because MSI is highly correlated with Lynch syndrome, and more recently has been associated with response to immune checkpoint inhibitor (ICI) therapeutics, several professional organizations recommend analysis of MSI and/or DNA mismatch repair protein expression (dMMR by IHC) for many different cancer types.[4–9]

Clinical oncology associations that endorse universal screening of colorectal and endometrial cancers for MSI to identify candidates for further diagnostic testing for Lynch syndrome include the European Society for Medical Oncology (ESMO), the National Comprehensive Cancer Network, and the American Society of Clinical Oncology.[4,5,9]

ESMO recognizes the importance of MSI and dMMR testing to support patient eligibility for ICI therapies. The recommendations surrounding MSI testing for this purpose has been summarized in the literature.[8,9]

The ESMO Translational Research and Precision Medicine Working Group recommends MSI testing on the spectrum of Lynch syndrome tumors because of the potential usefulness of ICI in these cancers and because the identification of Lynch syndrome can benefit extended family members. They recommend using MSI by PCR and dMMR by IHC together.

[4]National Comprehensive Cancer Network (www.nccn.org).

[5]Sepulveda, A.R. *et al.* (2017) Molecular Biomarkers for the Evaluation of Colorectal Cancer: Guideline From the American Society for Clinical Pathology, College of American Pathologists, Association for Molecular Pathology, and American Society of Clinical Oncology. *J. Mol. Diag.* **19**, 187–225.

[6]Le, D.T. *et al.* (2015) PD-1 Blockade in Tumors with Mismatch-Repair Deficiency. *New Engl. J. Med.* **372**, 2509–20.

[7]Le, D.T. *et al.* (2017) Mismatch-repair deficiency predicts response of solid tumors to PD-1 blockade. *Science* 10.1126/science.aan6733.

[8]Luchini, C. *et al.* (2019) ESMO recommendations on microsatellite instability testing for immunotherapy in cancer, and its relationship with PD-1/PD-L1 expression and tumour mutational burden: a systematic review-based approach. *Annals of Oncol Published online* May 6, 2019.

[9]Stjepanovic, N. *et al.* (2019) Hereditary gastrointestinal cancers: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol.,* **30**, 1558–71.

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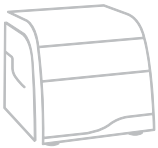
Tumor to Answer Overnight

The OncoMate™ MSI Dx Analysis System is part of a broader workflow that includes DNA extraction from formalin-fixed paraffin-embedded (FFPE) tissue samples, quantitation of DNA, amplification of specific microsatellite markers using multiplex PCR, fragment separation by capillary electrophoresis, and data analysis and interpretation.



Isolate DNA

from FFPE samples.

Quantitate DNA

using fluorescent DNA quantitation reagents and instruments.

Amplify DNA

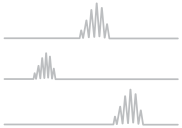
using the OncoMate™ MSI Dx Analysis System.

Calibrate the Dye Spectrum

using the OncoMate™ 5C Matrix Standard.

Separate and Detect Fragments

using a capillary electrophoresis instrument capable of fluorescent detection.



Data Analysis and Reporting

using fragment analysis software.

Turnaround Time: In as little as 10 hours or overnight

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Materials Required

- Less than one section each of normal and tumor FFPE tissue samples from the same individual
- A DNA extraction method *(e.g., Maxwell® CSC Instrument and Kits)*
- Double-stranded dye-based DNA quantitation method *(e.g., QuantiFluor® dsDNA System)*
- Thermocycler
- Capillary electrophoresis instrument
- OncoMate™ MSI Dx Analysis System
- OncoMate™ 5C Matrix Standard
- Fragment analysis software *(e.g., GeneMapper® Software)*

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Compatibility Specifications

Specimens

Normal and tumor FFPE tissue samples with a volume of 0.1–2.0mm^3. Tumor samples must contain at least 20% viable tumor cells.

DNA Quantity and Quality

Uses a target of 1ng per reaction, as estimated by a dsDNA binding dye or a qPCR system. These methods provide a reliable estimate of DNA concentration with highly fragmented DNA like that purified from FFPE.

Thermal Cycling

Use a thermal cycler that allows block ramp rates from 3.9°C to 5.0°C per second.

Data Analysis Software

Label (i.e., color), tabulate and display data from a mixture of fragment sizes (65bp to 300bp) and colors (5), and print and export analyzed data according to calculated allele size and marker.

Spectral Calibration

Prior to first use, perform a spectral calibration of the capillary electrophoresis instrument using the OncoMate™ 5C Matrix Standard (Cat.# MD3850).

Capillary Electrophoresis

Use with capillary electrophoresis instruments capable of:

- Fragment resolution of 1bp from 60bp to ≥300bp
- Sizing precision ≤0.15bp across a range from 60bp to ≥300bp.
- Calibration and detection of 5 channel collection with excitation wavelengths from 480nm to 520nm and detection optics to capture from approx. 500nm to 630nm.

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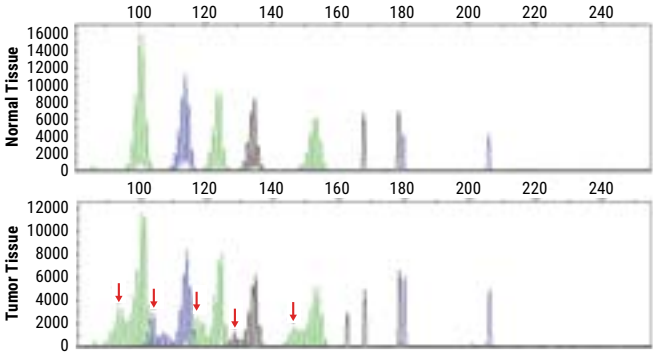
Biomarker and Loci Information

The OncoMate™ MSI Dx Analysis System includes fluorophore-labeled primers for co-amplification of seven microsatellite markers: five mononucleotide repeat markers (BAT-25, BAT-26, NR-21, NR-24 and MONO-27) and two pentanucleotide repeat markers (Penta C and Penta D).

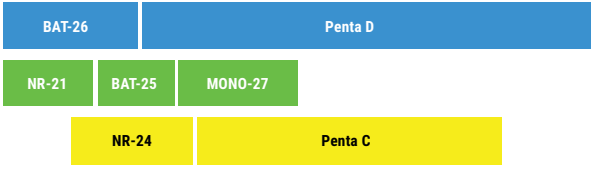
The mononucleotide-repeat markers are analyzed to determine MSI status and were selected for high sensitivity and specificity to alterations in repeat lengths in samples containing mismatch repair defects. The pentanucleotide-repeat markers were selected for their high level of polymorphism and are included as an identity check between individual normal and tumor sample pairs to confirm that the sample pairs were derived from the same individual.

Assay Type



Instability is determined by fragment size analysis on a capillary electrophoresis instrument following PCR amplification of DNA from a patient's normal and tumor tissue samples. Unstable loci in the tumor tissue are indicated by red arrows.

Target Markers



NCI recommended, Revised Bethesda Panel and two pentanucleotide markers.[10]

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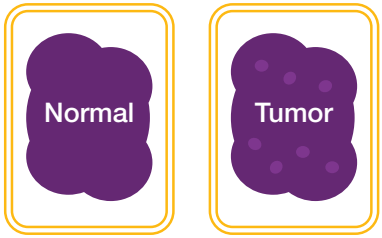
[10]Umar *et al.* (2004) Revised Bethesda Guidelines for hereditary nonpolyposis colorectal cancer (Lynch syndrome) and microsatellite instability. *J. Natl. Cancer Inst.* **96**, 261–8.

DNA Input Required

Uses only 1ng of amplification-quality DNA per reaction.

Tissue Requirement



Normal and tumor FFPE samples with tissue volume of 0.1mm^3 to 2.0mm^3. Tumor sample should contain at least 20% viable tumor cells.

Assay Time

Quick, multiplexed reaction, balanced for accuracy and efficiency, goes from DNA to answer in as little as 2.5 hours.

Be Efficient with your Precious Samples

The OncoMate™ MSI Dx Analysis System provides an MSI result with ≤1 FFPE section. A tumor sample with ≥20% tumor content can provide a valid result with the system.

In a study of colorectal cancers, the OncoMate™ MSI Dx Analysis System showed concordance with immunohistochemistry and is approved to help identify patients that may benefit from further diagnostic testing.

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What's in the Box

OncoMate™ MSI Dx Analysis System (Cat.# MD3140)

Item	Part #	Size
Water, Amplification Grade	MD193A	1 × 1,250µl
OncoMate™ MSI 5X Master Mix	MD280A	1 × 200µl
Size Standard 500	MD500A	1 × 100µl
OncoMate™ MSI 5X Primer Mix	MD705A	1 × 200µl
2800M Control DNA	MD810A	1 × 25µl

OncoMate™ 5C Matrix Standard (Cat.# MD3850)

Item	Part #	Size
Matrix Dilution Buffer	MD191A	5 × 200µl
5C Matrix Mix	MD430A	1 × 150µl

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Intended Use Statement:

The OncoMate™ MSI Dx Analysis System is a PCR-based fragment-sizing test used to determine microsatellite instability (MSI) status in DNA purified from human formalin-fixed paraffin-embedded (FFPE) tissue samples derived from solid tumors.

The OncoMate™ MSI Dx Analysis System generates allelic profiles from tumor and non-tumor FFPE tissue samples from the same patient through polymerase chain reaction (PCR) amplification of DNA microsatellite markers, followed by size separation of the amplified markers using capillary electrophoresis. MSI status is determined by comparing the allelic profiles. An expansion or reduction in the length of repetitive DNA sequences in the tumor cell DNA when compared to the normal cell DNA from the same patient indicates MSI. Normal and tumor tissue from the same patient must be tested at the same time and data from both samples must be available for comparison for results to be valid.

The OncoMate™ MSI Dx Analysis System is not intended to diagnose a specific disease. It is intended for use with patients already diagnosed with cancer who may benefit from additional genetic testing. Test results obtained using the product must be interpreted by healthcare professionals in conjunction with other clinical findings, family history and laboratory data. This product is intended for professional use only.

[a] U.S. Pat. Nos. 7,749,706 and 7,902,343

[b] U.S. Pat. No. 9,139,868, European Pat. No. 2972229 and other patents pending.

[c] TMR-ET, CXR-ET and WEN dyes are proprietary.

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If you have any questions, contact our Technical Services Team at:
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If you need access to medical information and resources, contact our Medical Affairs Team at:
MedicalAffairs@promega.com

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