

Microsatellite Instability (MSI) Testing

Test Code: MSI

Use: Evaluation of tumor tissue for microsatellite instability (MSI) has prognostic implications and is useful for detecting mismatch repair deficiency.

Clinical Significance: MSI testing is useful for identifying tumor tissues with defective mismatch repair. Mismatch repair deficiency may be due to Lynch Syndrome but can also be associated with sporadic methylation of the *MLH1* gene promoter. Identification of microsatellite instability – high (MSI-H) tumors will help identify individuals at risk of having Lynch Syndrome. Lynch Syndrome is a hereditary cancer syndrome predominately associated with increased risk of colorectal and endometrial carcinomas. At risk individuals may benefit from additional testing and/or genetic counseling; MSI testing is not diagnostic of Lynch Syndrome. Test results should be considered in conjunction with clinical and family history as well as with results of additional molecular testing, such as BRAF mutation testing and MLH1 promoter methylation testing. In colorectal cancers, MSI-H is also associated with an improved prognosis.

Methodology: PCR is used to amplify 5 mononucleotide microsatellite markers (BAT-25, BAT-26, NR-21, NR-24, and MONO-27) and 2 pentanucleotide microsatellite markers (Penta C and Penta D). Fluorescent PCR products are separated using capillary electrophoresis. The test is performed separately for the patient tumor and normal samples. Observed allele peaks generated from the tumor sample are compared to those generated from the normal sample. The appearance of novel peaks in at least 2 of the 5 mononucleotide microsatellite markers is interpreted as MSI-High. The appearance of novel peaks in only one marker is interpreted as MSI-Low. Microsatellite stability (MSS) means that no new allele peaks are seen in the tumor sample as compared to normal. Observed allele peaks at the pentanucleotide markers in the tumor sample are also compared to normal to ensure sample identity. Allele identification is sensitive down to two nanograms of input DNA. Before testing, adequate quality and quantity of DNA extracted from the sample is confirmed. Acceptable results from positive and negative controls are necessary for interpretation.

Reference Range: Microsatellite Stable (MSS)

Reportable Range: Microsatellite Stable (MSS), Microsatellite Instability – Low (MSI-L), and Microsatellite Instability – High (MSI-H).

Assay Availability: Batched weekly

Results Reported: 7 days

Specimen: Formalin fixed paraffin embedded tissue for normal and tumor.

Volume: One H&E slide and at least 2 unstained slides for both tumor and normal. More unstained slides may be necessary for small biopsy tissues and cytology cell blocks.

Storage: Tissue blocks can be stored at room temperature.

Causes for Rejection: Insufficient tumor cellularity (<15%); decalcified specimens; specimens treated with Bouin's, B5, or other fixatives.

Laboratory Contact: For further information, please call the Molecular Diagnostics Laboratory at (501) 526-6439.