The MSH2 protein, encoded by the MSH2 gene, is one of the key components of the mismatch repair system. This system is crucial for maintaining genetic stability, as it corrects errors that occur during DNA replication or repair. Mutations in the MSH2 gene contribute to the development of sporadic colorectal cancer (CRC). The repair of mismatch DNA is essential in the MSH2 gene for maintaining the integrity of genetic information over time. An alteration of the MSH2 protein can lead to the development of CRC, making MSH2 a predictive marker for this disease.

MSH2 is a 100 kDa nuclear antigen and encodes a protein of 934 amino acids. The MSH2 gene is one of only 4 known to encode proteins involved in the MSH2 repair of mismatch nucleotides following DNA replication or repair. Mutations of MLH1 and PMS2 (MLH1/PMS2 deleted) have shown objective response to PD-L1 inhibitors, with published clinical data suggesting that this antibody has been demonstrated to be a useful predictive marker for anti-PD-L1 immunotherapy in colorectal carcinoma (3).

**Intended Use:**
For In Vitro Diagnostic Use

**MSH2** [FE11] is a mouse monoclonal antibody that is intended for laboratory use in the qualitative identification of MSH2 protein by immunohistochemistry (IHC) in formalin-fixed paraffin-embedded (FFPE) human tissues. The clinical interpretation of any staining or its absence should be complemented by morphological studies using proper controls and should be evaluated within the context of the patient's clinical history and other diagnostic tests by a qualified pathologist.

**Summary and Explanation:**
MSH2 is a 100 kDa nuclear antigen and encodes a protein of 934 amino acids. The MSH2 gene is one of only 4 known to encode proteins involved in the repair of mismatch nucleotides following DNA replication or repair. Mutations in the MSH2 gene contribute to the development of sporadic colorectal carcinoma. MSH2 mutations are responsible for 50% of hereditary non-polyposis colorectal cancer (HNPCC). The repair of mismatch DNA is essential to maintaining the integrity of genetic information over time. An alteration of microsatellite repeats is the result of slippage owing to strand misalignment during DNA replication and is referred to as microsatellite instability (MSI). These defects in DNA repair pathways have been related to human carcinogenesis. MSH2 is involved in the initial cognizance of mismatch nucleotides during the replication mismatch repair process. It is thought that after MSH2 binds to a mismatched DNA duplex it is joined by a heterodimer of MLH1 and PMS2, which together help facilitate the later steps in mismatch repair. Patients with colorectal carcinoma that is mismatch-repair-deficient and confirmed with immunohistochemistry (IHC) (MSH2/MSH6 negative or MLH1/PMS2 deleted) have shown objective response to PD-1 antibody, pembrolizumab (2). PD-L1 IHC test has been demonstrated to be a useful predictive marker for anti-PD-1 immunotherapy in colorectal carcinoma (3).

**Principle of Procedure:**
Antigen detection in tissues and cells is a multi-step immunohistochemical process. The initial step binds the primary antibody to its specific epitope. After labeling the antigen with a primary antibody, a one-, two- or three-step detection procedure can be employed. The one-step procedure will feature an enzyme-labeled polymer that binds to the primary antibody. A two-step procedure will feature a secondary antibody added to bind to the primary antibody. An enzyme-labeled polymer is then added to bind to the secondary antibody. The three-step detection procedure will feature a secondary antibody added to bind to the primary antibody followed by a linker antibody step for maximum binding. An enzyme-labeled polymer is then added to bind to the linker antibody. These detections of the bound antibodies are evidenced by a colorimetric reaction.

**Source:** Mouse monoclonal

**Species Reactivity:** Human, mouse and rat

**Clone:** FE11

**Isotype:** IgG1/kappa

**Protein Concentration:** Call for lot specific Ig concentration.

**Epitope/Antigen:** MSH2

**Cellular Localization:** Nuclear

**Positive Tissue Control:** Colon cancer

**Known Applications:** Immunohistochemistry (formalin-fixed paraffin-embedded tissues)

**Supplied As:** Buffer with protein carrier and preservative

**Renoir Red Diluent (PD904)**

**Storage and Stability:**
Store at 2ºC to 8ºC. The product is stable to the expiration date printed on the label, when stored under these conditions. Do not use after expiration date. Diluted reagents should be used promptly; any remaining reagent should be stored at 2ºC to 8ºC.

**Protocol Recommendations (VALENT® Automated Slide Staining Platform):**
VLTM219 is intended for use with the VALENT. Refer to the User Manual for specific instructions for use. Protocol parameters in the Protocol Manager should be programmed as follows:

- DenaRenparationization: DenaRenparationize for 8 minutes with Val DePar.
- Pretreatment: Perform heat retrieval at 98°C for 60 minutes using Val AR-Hi pH, 5X (use at 1X).
- Enzyme: Incubate for 10 minutes with Val Zyme Trypsin (1:50 mix)
- Peroxidase Block: Block for 5 minutes with Val Peroxidase Block.
- Protein Block (Optional): Incubate for 10-20 minutes at RT with Val Backround Block.
- Primary Antibody: Incubate for 30 minutes.
- Secondary: Incubate for 10 minutes with Val Mouse Secondary.
- Linker: Incubate for 10 minutes with Val Universal Linker.
- Polymer: Incubate for 10 minutes with Val Universal Polymer.
- Chromogen: Incubate for 5 minutes with Val DAB.
- Counterstain: Counterstain for 5 minutes with Val Hematoxylin.

**Protocol Recommendations (intelliPATH FLX® and manual use):**

- Peroxide Block: Block for 5 minutes with Peroxidazed L.
- Pretreatment: Perform heat retrieval using Diva Decloaker. Refer to the Diva Decloaker data sheet for specific instructions.
- Protein Block (Optional): Incubate for 5-10 minutes at RT with Background Punisher.
- Primary Antibody: Incubate for 30 minutes at RT.
- Probe: Incubate for 10 minutes at RT with a secondary probe.
- Polymer: Incubate for 10-20 minutes at RT with a tertiary polymer.
- Chromogen: Incubate for 5 minutes at RT with Biocare's DAB-OR-Incubate for 5-7 minutes at RT with Warp Red.
- Counterstain: Counterstain with hematoxylin. Rinse with deionized water. Apply Tacha's Bluing Solution for 1 minute. Rinse with deionized water.

**Technical Note:**
This antibody, for intelliPATH FLX and manual use, has been standardized with MACH 4 detection system. Use TBS for washing steps.

**Protocol Recommendations (ONCORE™ Automated Slide Staining Platform):**
OA129 is intended for use with the ONCORE. Refer to the User Manual for specific instructions for use. Protocol parameters in the Protocol Editor should be programmed as follows:

- **Protocol Name:** MSH2
- **Protocol Template (Description):** Ms HRP Template 1
Precautions Cont'd:

2. Specimens, before and after fixation, and all materials exposed to them should be handled as if capable of transmitting infection and disposed of with proper precautions. Never pipette reagents by mouth and avoid contacting the skin and mucous membranes with reagents and specimens. If reagents or specimens come in contact with sensitive areas, wash with copious amounts of water. (5)

3. Microbial contamination of reagents may result in an increase in nonspecific staining.

4. Incubation times or temperatures other than those specified may give erroneous results. The user must validate any such change.

5. Do not use reagent after the expiration date printed on the vial.

6. The SDS is available upon request and is located at http://biocare.net.

Troubleshooting:

Follow the antibody specific protocol recommendations according to data sheet provided. If atypical results occur, contact Biocare’s Technical Support at 1-800-542-2002.

References:


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