PMS2

Concentrated and Prediluted Monoclonal Antibody
901-344-122320

BIOCARE MEDICAL

Available Product Formats				
Format	Catalog Number	Description	Dilution	Diluent
Concentrate	CM 344 AK, BK	0.1, 0.5 mL	1:100	Renoir Red
Predilute	PM 344 AA, H	6.0, 25 mL	Ready-to-use	N/A
intelliPATH FLX	IPI 344 G10	10 mL	Ready-to-use	N/A
ONCORE	OAI 344 T60	60 tests	Ready-to-use	N/A
ONCORE Pro	OPAI 344 T60	60 tests	Ready-to-use	N/A
VALENT	VLTM 344 G20	20 mL	Ready-to-use	N/A
UltraLine – For BenchMark	AVI 344 G	6.0 mL	Ready-to-use	N/A

Intended Use:
For In Vitro Diagnostic Use
PMS2 [A16-4] is a mouse monoclonal antibody that is intended for laboratory use in the qualitative identification of PMS2 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:
The PMS2 post meiotic segregation increased 2 gene is located on chromosome number 7. The gene product of PMS2 forms a heterodimer with MLH1 that interacts with MSH2 bound to mismatched bases in DNA. MSH2 is a protein of 934 aa (100 kDa) localized to the cell nucleus. MSH2 functions as one of the four major DNA mismatch repair genes along with PMS2, MLH1 and PMS1. Mutations in these genes are associated with hereditary nonpolyposis colon cancer (HNPCC), one of the most common hereditary diseases in man. Immunohistochemistry studies have further determined that the microsatellite instability phenotype in endometrial carcinoma is linked to defects in the MLH1/PMS2 gene. 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 (6). PD-L1 IHC test has been demonstrated to be a useful predictive marker for anti-PD-1 immunotherapy in colorectal carcinoma (7).

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; others not tested
Clone: A16-4
Isotype: IgG1/kappa
Protein Concentration: Call for lot specific Ig concentration.
Epitope/Antigen: PMS2
Cellular Localization: Nuclear
Positive Tissue Control: Placenta, 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):
VLTM344 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:
Deparaffinization: Deparaffinize 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 Background 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 1.
Pretreatment: Perform heat retrieval using Borg or Reveal Decloaker. Refer to the Borg or Reveal Decloaker product data sheet for specific instructions.
Protein Block (Optional): Incubate for 5-10 minutes at RT with Background Punisher.
Primary Antibody: Incubate for 30-60 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.
intelliPATH FLX Automated Slide Stainer:
IPI344 is intended for use on the intelliPATH FLX. Refer to the User Manual for specific instructions for use. When using the intelliPATH FLX, peroxide block with intelliPATH FLX Peroxidase Blocking Reagent (IPB5000) may be performed following heat retrieval.
Technical Note:
This antibody, for intelliPATH FLX and manual use, has been standardized with MACH 4 detection system. Use TBS for washing steps.

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Protocol Recommendations (ONCORE™ Automated Slide Staining System):

OAI344 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: PMS2
Protocol Template (Description): IHC Extras Template
Dewaxing (DS Option): DS2
Antigen Retrieval (AR Option): AR1, high pH; 103°C
Reagent Name, Time, Temp.: PMS2, 30 min., 25°C
- Use of **Mouse Amp HRP Detection (ORI6050)** is required for the above antibody protocol. Mouse HRP Detection (ORI6007) is not recommended.

Protocol Recommendations (ONCORE™ Pro Automated Slide Staining System):

OPAI344 is intended for use with the ONCORE Pro. Refer to the User Manual for specific instructions for use. Protocol parameters in the Protocol Editor should be programmed as follows:
Protocol Name: PMS2
Protocol Template (Description): IHC Extras Template 1
Dewaxing (DS Buffer Option): DS2-50
Antigen Retrieval (AR Option): AR1, high pH; 103°C
Block Option: Buffer
Reagent Name, Time, Temp.: PMS2, 30 min., 25°C
- Use of **Mouse Amp HRP Detection (OPRI6050) is required** for the above antibody protocol. Mouse HRP Detection (OPRI6007) is not recommended.

Protocol Recommendations (Ventana BenchMark ULTRA):

AVI344 is intended for use with the BenchMark ULTRA. Refer to the User Manual for specific instructions for use. Recommended protocol parameters are as follows:
Template/Detection: OptiView DAB IHC 12 minutes, 12 minutes
Pretreatment Protocol: CC2 92 minutes, 100°C
Peroxidase: Pre Primary Peroxidase Inhibitor
Option (V-Blocker BRI4001): Incubate for 4 minutes (with appropriate Option # registered by user)
V-Blocker is recommended to be applied prior to any primary antibody.
Primary Antibody: 36 minutes, No Heat
Amplification Kit: Incubate 4 minutes with Amplification HQ Linker and 4 minutes with Amplification Multimer.

Limitations:

The optimum antibody dilution and protocols for a specific application can vary. These include, but are not limited to fixation, heat-retrieval method, incubation times, tissue section thickness and detection kit used. Due to the superior sensitivity of these unique reagents, the recommended incubation times and titers listed are not applicable to other detection systems, as results may vary. The data sheet recommendations and protocols are based on exclusive use of Biocare products. Ultimately, it is the responsibility of the investigator to determine optimal conditions.

Quality Control:

Refer to CLSI Quality Standards for Design and Implementation of Immunohistochemistry Assays; Approved Guideline-Second edition (I/LA28-A2). CLSI Wayne, PA, USA (www.clsi.org). 2011

Precautions:

1. This antibody contains less than 0.1% sodium azide. Concentrations less than 0.1% are not reportable hazardous materials according to U.S. 29 CFR 1910.1200, OSHA Hazard communication and EC Directive 91/155/EC. Sodium azide (NaN_3) used as a preservative is toxic if ingested. Sodium azide may react with lead and copper plumbing to form highly explosive metal azides. Upon disposal, flush with large volumes of water to prevent azide build-up in plumbing. (Center for Disease Control, 1976, National Institute of Occupational Safety and Health, 1976) (8)
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. (9)
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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2. Modica I, *et al.* Utility of immunohistochemistry in predicting microsatellite instability in endometrial carcinoma. Am J Surg Pathol. 2007 May;31(5):744-51.
3. Sordet C, Goetz J, Sibilia J. Contribution of autoantibodies to the diagnosis and nosology of inflammatory muscle disease. Joint Bone Spine. 2006 Dec;73(6):646-54.
4. Balogh GA, Heulings RC, Russo J. The mismatch repair gene hPMS2 is mutated in primary breast cancer. Int J Mol Med. 2006 Nov;18(5): 853-7.
5. Halvarsson B, *et al.* The added value of PMS2 immunostaining in the diagnosis of hereditary nonpolyposis colorectal cancer. Fam Cancer. 2006;5(4):353-8.
6. Lee, LH, *et al.* Patterns and prognostic relevance of PD-1 and PD-L1 expression in colorectal carcinoma. Mod Pathol. 2016;29:1333-42.
7. Le, DI, *et al*. PD-1 blockade in tumors with mismatch-repair deficiency. N Engl J Med. 2015;372:2509-20.
8. Center for Disease Control Manual. Guide: Safety Management, NO. CDC-22, Atlanta, GA. April 30, 1976 "Decontamination of Laboratory Sink Drains to Remove Azide Salts."
9. Clinical and Laboratory Standards Institute (CLSI). Protection of Laboratory Workers from Occupationally Acquired Infections; Approved Guideline-Fourth Edition CLSI document M29-A4 Wayne, PA 2014.

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