Mesothelin

Concentrated and Prediluted Monoclonal Antibody
901-3175-073117

BIOCARE MEDICAL

Catalog Number:	**ACI 3175 A, B**	**API 3175 AA**
Description:	0.1, 0.5 ml, concentrated	6.0 ml, prediluted
Dilution:	1:100	Ready-to-use
Diluent:	Renoir Red	N/A

Intended Use:

For In Vitro Diagnostic Use

Mesothelin [MSLN-15C11] is a mouse monoclonal antibody that is intended for laboratory use in the qualitative identification of mesothelin 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:

Mesothelin is a cell surface glycoprotein that elicits T cell responses, first described as the antigenic target of the K1 monoclonal antibody, generated by using an ovarian cell line as immunogen (1,7). In normal tissues, mesothelin expression is largely restricted to mesothelial cells. However, immunoreactivity for this marker has also been reported in some epithelial cells of the trachea, tonsil, kidney, and fallopian tube (1).

Mesothelin is one of the most sensitive markers for mesothelioma, and it has been reported to be expressed in all or nearly all epithelioid mesotheliomas as well as in some carcinomas, particularly those arising in the ovary (serous carcinomas) and pancreas (1-7). Epithelioid mesotheliomas and adenomatoid tumors invariably express mesothelin, and the reaction is usually strong and diffuse and occurs along the cell membrane. This is in contrast to sarcomatoid mesotheliomas, which are usually negative for this marker (6,8). Among carcinomas, most pancreatic adenocarcinomas (86%-100%) and nonmucinous carcinomas of the ovary, including serous carcinomas (93%-100%), clear cell carcinomas (43%-75%), and transitional cell carcinomas (100%), have been reported to be mesothelin positive (8). Approximately 40% to 50% of pulmonary adenocarcinomas and 15% to 30% of squamous cell carcinomas of the lung have also been reported to express this marker in a focal and cytoplasmic staining pattern, in contrast to mesotheliomas' membranous pattern (4,5,8).

Even with the low specificity for mesothelioma, the common strong membranous reactivity in epithelioid mesotheliomas should be regarded as a strong indication against the diagnosis of mesothelioma when a negative stain is achieved (3). In addition, because mesothelin expression has been reported to be either negative or rarely weakly positive in some carcinomas, such as renal cell carcinomas, it may be included in the panel of markers used to distinguish these tumors from epithelioid mesotheliomas (5,8).

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 secondary antibody is added to bind to the primary antibody. An enzyme label is then added to bind to the secondary antibody; this detection of the bound antibody is evidenced by a colorimetric reaction.

Source: Mouse monoclonal
Species Reactivity: Human; others not tested
Clone: MSLN-15C11
Isotype: IgG1/kappa
Total Protein Concentration: ~10 mg/ml. Call for lot specific Ig concentration.
Epitope/Antigen: Mesothelin
Cellular Localization: Membranous for mesotheliomas; cytoplasmic for carcinomas
Positive Tissue Control: Lung and fallopian tube
Known Applications:
Immunohistochemistry (formalin-fixed paraffin-embedded tissues)
Supplied As: Buffer with protein carrier and preservative
Storage and Stability:
Store at 2ºC to 8ºC. Do not use after expiration date printed on vial. If reagents are stored under conditions other than those specified in the package insert, they must be verified by the user. Diluted reagents should be used promptly; any remaining reagent should be stored at 2ºC to 8ºC.

Protocol Recommendations:

Peroxide Block: Block for 5 minutes with Biocare's Peroxidazed 1.
Pretreatment: Perform heat retrieval using Biocare's Diva Decloaker. Refer to the Diva Decloaker data sheet for specific instructions.
Protein Block (Optional): Incubate for 5-10 minutes at RT with Biocare's 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 Biocare's 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 has been standardized with Biocare's MACH 4 detection system. Use TBS buffer for washing steps.
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. The clinical interpretation of any positive or negative staining should be evaluated within the context of clinical presentation, morphology and other histopathological criteria by a qualified pathologist. The clinical interpretation of any positive or negative staining should be complemented by morphological studies using proper positive and negative internal and external controls as well as other diagnostic tests.
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

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Precautions Cont'd:
volumes of water to prevent azide build-up in plumbing. (Center for Disease Control, 1976, National Institute of Occupational Safety and Health, 1976) (9)
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 into contact with sensitive areas, wash with copious amounts of water. (10)
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:
1. Chang K, *et al*. Isolation and characterization of a monoclonal antibody, K1, reactive
with ovarian cancers and normal mesothelium. Int J Cancer. 1992 Feb 1;50(3):373-81.
2. Ordóñez NG. The immunohistochemical diagnosis of mesothelioma: a comparative study of epithelioid mesothelioma and lung adenocarcinoma. Am J Surg Pathol. 2003 Aug;27(8):1031-51.
3. Ordóñez NG. Value of mesothelin immunostaining in the diagnosis of mesothelioma. Mod Pathol. 2003 Mar;16(3):192-7.
4. Frierson HF Jr, *et al*. Large-scale molecular and tissue microarray analysis of mesothelin expression in common human carcinomas. Hum Pathol. 2003 Jun;34(6):605 -9.
5. Ordóñez NG. Application of mesothelin immunostaining in tumor diagnosis. Am J Surg Pathol. 2003 Nov;27(11):1418-28.
6. Ordóñez NG. The diagnostic utility of immunohistochemistry in distinguishing between mesothelioma and renal cell carcinoma: a comparative study. Hum Pathol. 2004 June;35(6):697-710.
7. Tchou J, *et al*. Mesothelin, a novel immunotherapy target for triple negative breast cancer. Breast Cancer Res Treat. 2012 Jun;133(2):799-804.
8. Ordóñez NG. Application of immunohistochemistry in the diagnosis of epithelioid mesothelioma: a review and update. Hum Pathol. 2013 Jan;44(1):1-19.
9. 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."
10. 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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