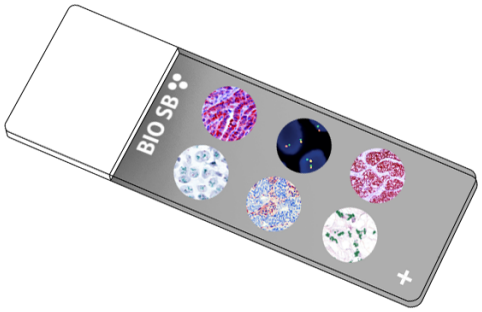
ATM
Control Slides

CE IVD



Intended Use
For In Vitro Diagnostic Use.

Summary and Explanation
Ataxia telangiectasia mutated protein is a serine/threonine kinase that belongs to the family of phosphatidylinositol-3 kinase-related protein kinases. ATM is a key checkpoint protein of the DNA damage response pathway. When DNA double-strand breaks occur, ATM activates different cascades, resulting in activation of cell cycle checkpoints, cell cycle arrests, and apoptosis.

Mutations in the ATM gene lead to an increased risk of several cancer types, which include Leukemias, Lymphomas, Colorectal Cancer, Pancreatic Cancer and Adenocarcinoma of the Stomach. Studies show that Gastric Cancer tissues were found to be ATM-negative by IHC staining, indicating that ATM can be used as a biomarker. It has also been found that low expression of the ATM protein contributes to more aggressive progression and poor clinical outcome of Breast Cancer. Results of another study indicate loss of ATM protein expression is associated with development of Lung Cancer.

Presentation
Five slides of ATM positive tissues, each mounted on Hydrophilic Plus Slides, provided in a plastic mailer.

Catalog No.	*Quantity*
BSB-9021-CS	5 slides
BSB-3710-CS	5 slides

Storage Store at 20-25°C

Precautions
1. For professional users only. Results should be interpreted by a qualified medical professional.
2. Ensure proper handling procedures are used with this reagent.
3. Always wear personal protective equipment such as a laboratory coat, goggles, and gloves when handling reagents.
4. Dispose of unused solution with copious amounts of water.
5. Follow safety precautions of the heating device used for epitope retrieval (TintoRetriever Pressure Cooker or similar).
8. For additional safety information, refer to Safety Data Sheet for this product.
9. For complete recommendations for handling biological specimens, please refer to the CDC document, "Guidelines for Safe Work Practices in Human and Animal Medical Diagnostic Laboratories" (see References in this document).

Stability
This product is stable up to the expiration date on the product label.
Do not use after expiration date listed on package label.

IHC Protocol
1. Subject tissues to heat induced epitope retrieval (HIER) using a suitable retrieval solution such as ImmunoDNA Retriever with Citrate (BSB 0020-BSB 0023) or EDTA (BSB 0030-BSB 0033).
2. Any of three heating methods may be used:
a. TintoRetriever Pressure Cooker or Equivalent
Place tissues/slides in a staining dish or coplin jar containing the ImmunoDNA Retriever with Citrate or EDTA and place on trivet in the pressure cooker. Add 1-2 inches of distilled water to the pressure cooker and turn heat to high. Incubate for 15 minutes. Open and immediately transfer slides to room temperature.
b. TintoRetriever PT Module or Water Bath Method
Place tissues/slides in a pre-warmed staining dish or coplin jar containing the ImmunoDNA Retriever with Citrate or EDTA at 95°-99° C. Incubate for 30-60 minutes.
c. Conventional Steamer Method
Place tissues/slides in a pre-warmed staining dish or coplin jar containing the ImmunoDNA Retriever with Citrate or EDTA in a steamer, cover and steam for 30-60 minutes.
3. After heat treatment, transfer slides in ImmunoDNA Retriever with Citrate or EDTA to room temperature and let stand for 15-20 minutes.
4. For manual staining, perform antibody incubation at ambient temperature. For automated staining methods, perform antibody incubation according to instrument manufacturer's instructions.
5. Wash slides with ImmunoDNA washer or DI water.
6. Continue IHC staining protocol. Wash slides between each step with ImmunoDNA washer solution.

Abbreviated Immunohistochemical Protocol

Step	ImmunoDetector AP/HRP	PolyDetector AP/HRP	PolyDetector Plus HRP
Peroxidase/AP Blocker	5 min.	5 min.	5 min
Primary Antibody	30-60 min.	30-60 min.	30-60 min.
1st Step Detection	10 min.	30-45 min.	15 min.
2nd Step Detection	10 min.	Not Applicable	15 min.
Substrate- Chromogen	5-10 min.	5-10 min.	5-10 min.
Counterstain / Coverslip	Varies	Varies	Varies

Abbreviated IF Protocol

Step	Incubation Time
Rinse slides in IF wash buffer	5 minutes
Drain and wipe excess IF wash buffer off slide	
Conduct remaining steps in the dark	
Apply Antibody	30-60 minutes
Rinse with 3 changes of IF wash buffer	3x15 minutes each
Coverslip with IF mounting medium	

Mounting Protocols

For detailed instructions using biodegradable permanent mounting media such as XyGreen PermaMounter (BSB 0169-0174) or organic solvent based resin such as PermaMounter (BSB 0094-0097), refer to PI0174 or PI0097.

Product Limitations

Due to inherent variability present in immunohistochemical procedures (including fixation time of tissues, dilution factor of antibody, retrieval method utilized, and incubation time), optimal performance should be established through the use of positive and negative controls. Results should be interpreted by a qualified medical professional.

References

1. Nanda N, Roberts NJ. ATM Serine/Threonine Kinase and its Role in Pancreatic Risk. Genes (Basel). 2020;11(1):108. Published 2020 Jan 17. doi:10.3390/genes110101082. Sundar R, Miranda S, Rodrigues DN, et al. Ataxia Telangiectasia Mutated Protein Loss and Benefit From Oxaliplatin-based Chemotherapy in Colorectal Cancer. Clin Colorectal Cancer. 2018;17(4):280-284. doi:10.1016/j.clcc.2018.05.0113. Mavrou A, Tsangaris GT, Roma E, Kolialexi A. The ATM gene and ataxia telangiectasia. Anticancer Res. 2008;28(1B):401-405.4. Miller RM, Nworu C, McKee L, et al. Development of an Immunohistochemical Assay to Detect the Ataxia-Telangiectasia Mutated (ATM) Protein in Gastric Carcinoma. Appl Immunohistochem Mol Morphol. 2020;28(4):303-310. doi:10.1097/PAI.0000000000007865. Kim HS, Kim MA, Hodgson D, et al. Concordance of ATM (ataxia telangiectasia mutated) immunohistochemistry between biopsy or metastatic tumor samples and primary tumors in gastric cancer patients. Pathobiology. 2013;80(3):127-137. doi:10.1159/0003460346. Feng X, Li H, Dean M, et al. Low ATM protein expression in malignant tumor as well as cancer-associated stroma are independent prognostic factors in a retrospective study of early-stage hormone-negative breast cancer. Breast Cancer Res. 2015;17(1):65. Published 2015 May 3. doi:10.1186/s13058-015-0575-27. Petersen LF, Klimowicz AC, Otsuka S, et al. Loss of tumour-specific ATM protein expression is an independent prognostic factor in early resected NSCLC. Oncotarget. 2017;8(24):38326-38336. doi:10.18632/oncotarget.162158. U.S. Department of Health and Human Services: Centers for Disease Control and Prevention. Guidelines for Safe WorkPractices in Human and Animal Medical Diagnostic Laboratories. Supplement / Vol. 61, January 6, 2012. https://www.cdc.gov/mmwr/pdf/other/su6101.pdf

Symbol Key / Légende des symboles/Erläuterung der Symbole

EC REP EMERGO EUROPE Prinsessegracht 20 2514 AP The Hague The Netherlands	Storage Temperature Limites de température Zulässiger Temperaturbereich	Manufacturer Fabricant Hersteller	REF Catalog Number Référence du catalogue Bestellnummer
IVD In Vitro Diagnostic Medical Device Dispositif médical de diagnostic in vitro In-Vitro-Diagnostikum	Read Instructions for Use Consulter les instructions d'utilisation Gebrauchsanweisung beachten	Expiration Date Utiliser jusque Verwendbar bis	LOT Lot Number Code du lot Chargenbezeichnung

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