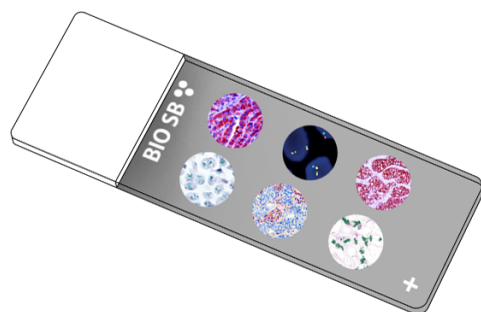


Thymidylate synthase/TS

Control Slides



Intended Use

For In Vitro Diagnostic Use.

Summary and Explanation

Thymidylate synthase catalyzes the methylation of deoxyuridine monophosphate to deoxythymidine monophosphate using 5, 10-methylenetetrahydrofolate as a cofactor. This enzyme is critical for DNA repair and replication. Polymorphism of the gene TYMS, which encodes TS, may be associated with etiology of neoplasia and responses to chemotherapy. TS inhibitors like 5-fluorouracil have been successful in down-regulating tumor progression and increasing immune responses in pancreatic, breast, gastric, ovarian, lung, and head & neck cancer. A study reported TS protein expression and gene copy number were assayed using IHC and silver in situ hybridization, respectively, on primary tumors of resected non-small cell lung cancer patients and concluded that TS protein expression and gene copy number vary widely in non-small cell lung cancer and correlate significantly to each other. TS gene copy number is higher in SCCs, whereas TS protein expression does not associate with histological subtypes, clinical features or survival. Variability of TS protein expression and gene copy number may indicate potential benefit from protein expression pemetrexed therapy in selected SCC patients. A number of studies have investigated the relationship between thymidylate synthase expression and survival in colorectal cancer patients. Most have reported poorer overall and progression-free survival with high TS expression. Another study suggests that immunostaining for TS and p53 protein is useful for pretreatment selection of gastric cancer patients unresponsive to S-1/cisplatin chemotherapy.

Presentation

Five slides of Thymidylate synthase/TS positive tissues, each mounted on Hydrophilic Plus Slides, provided in a plastic mailer.

Catalog No.	Quantity
BSB-9406-CS	5 slides
BSB-3750-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 the 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 PermaMunter (BSB 0169-0174) or organic solvent based resin such as PermaMunter (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

- Fu Z, Jiao Y, Li Y, Ji B, Jia B, Liu B. TYMS presents a novel biomarker for diagnosis and prognosis in patients with pancreatic cancer. *Medicine* (Baltimore). 2019;98(51):e18487. doi:10.1097/MD.000000000000184872. Qi C, Gao H, Li S, Zong H, Hao H, Zhang L. A Case-Control Study on the Correlation Between Thymidylate Synthase Gene Polymorphisms and Raltitrexed Treatment Combined with Transcatheter Arterial Chemoembolization in Hepatocellular Carcinoma Treatment. *Genet Test Mol Biomarkers*. 2020;24(3):156-164. doi:10.1089/gtmb.2019.01113. Guo R, Tian Y, Jin X, Huang X, Yang J. Thymidylate Synthase, a New Myoepithelial Biomarker for Breast Lesions. *Int J Surg Pathol*. 2019;27(8):852-858. doi:10.1177/10668969198584034. Nicolini A, Conte M, Rossi G, et al. Additional 5-FU-LV significantly increases survival in gastrointestinal cancer. *Front Biosci (Elite Ed)*. 2011;3:1475-1482. Published 2011 Jun 1. doi:10.2741/e3485. Wynes MW, Konopa K, Singh S, et al. Thymidylate synthase protein expression by IHC and gene copy number by SISH correlate and show great variability in non-small cell lung cancer. *J Thorac Oncol*. 2012;7(6):982-992. doi:10.1097/JTO.0b013e31824fe95a6. Popat S, Matakidou A, Houlston RS. Thymidylate synthase expression and prognosis in colorectal cancer: a systematic review and meta-analysis. *J Clin Oncol*. 2004;22(3):529-536. doi:10.1200/JCO.2004.05.0647. Kamoshida S, Suzuki M, Shimomura R, et al. Immunostaining of thymidylate synthase and p53 for predicting chemoresistance to S-1/cisplatin in gastric cancer. *Br J Cancer*. 2007;96(2):277-283. doi:10.1038/sj.bjc.66035468. U.S. Department of Health and Human Services: Centers for Disease Control and Prevention. Guidelines for Safe Work Practices 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 QAdvis EAR AB Ideon Science Park Scheelevägen 17 SE-223 70 Lund, Sweden	 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