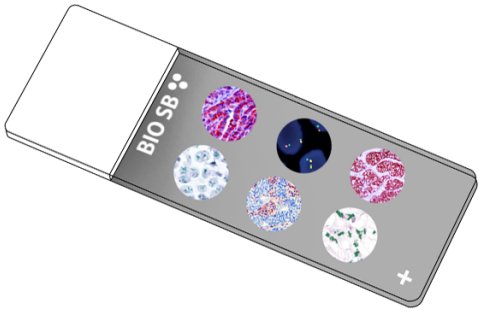
Glutamine Synthetase Control Slides

CE IVD



Intended Use
For In Vitro Diagnostic Use.

Summary and Explanation
Glutamine synthetase is an enzyme that plays an essential role in the metabolism of nitrogen by catalyzing the condensation of glutamate and ammonia to form glutamine. Glutamine synthetase is present predominantly in the brain, kidneys, and liver. Glutamine synthetase in the brain participates in the metabolic regulation of glutamate, the detoxification of brain ammonia, the assimilation of ammonia, recyclization of neurotransmitters, and termination of neurotransmitter signals. In normal liver, Glutamine synthetase expression is seen in pericentral hepatocytes, but not in mid-zonal or periportal hepatocytes.

Glutamine synthetase positive tumor cells are believed to be derived from Glutamine synthetase positive hepatocytes. Glutamine synthetase immunoreactivity has been seen in a majority of hepatocellular carcinoma, including cases of early hepatocellular carcinoma (70%) and for low grade hepatocellular carcinoma (59%).In nonmalignant nodules, Glutamine synthetase overexpression is only seen in high grade dysplastic nodules (HGDN, 13.6%). In these cases, Glutamine synthetase overexpression was restricted to 11.5%-50% of hepatocytes, whereas in hepatocellular carcinoma the majority of cases (53%), including early hepatocellular carcinoma (60%), showed diffuse immunostaining (>50% tumor cells). A panel composed of antibodies against HSP70, GPC3, and Glutamine synthetase has been proposed to be very useful in distinguishing between dysplastic and early malignant hepatocellular nodules arising in cirrhosis. Staining of hepatocellular lesions with anti-Glutamine synthetase antibody have been useful in the differential diagnosis of focal nodular hyperplasia (FNH), hepatic adenoma (HCA), and dysplastic nodules, and low grade hepatocellular carcinoma. In the case of FNH, Glutamine synthetase stains in a characteristic "map-like" pattern, thus differentiating it from HCA, in which Glutamine synthetase staining is usually absent, but may occasionally be present at the border of the lesion or around the veins inside the tumor.

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

Catalog No.	*Quantity*
BSB-9198-CS	5 slides
BSB 2935	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. Eisenberg D, et al. Some evolutionary relationships of the primary biological catalysts glutamine synthetase and RuBisCO. Cold Spring Harb. Symp. Quant. Biol. 1987; 52: 483–90.
2. Liaw SH, Kuo I, Eisenberg D. Discovery of the ammonium substrate site on glutamine synthetase, a third cation bindinGlutamine synthetaseite. Protein Sci. 1995; 4 (11): 2358–65.
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4. Bioulac-Sage P et al. Over-expression of glutamine synthetase in focal nodular hyperplasia: a novel easy diagnostic tool in surgical pathology. Liver International. 2009; 3:459-465.
5. Shafizideh N, Kakar S. Diagnosis of well-differentiated hepatocellular lesions: role of immunohistochemistry and other ancillary techniques. Adv Anat Pathol. 2011; 18: 438-445.
6. Bioulac-Sage, P et al. Immunohistochemical markers on needle biopsies are helpful for the diagnosis of focal nodular hyperplasia and hepatocellular adenoma subtypes. Am J Surg Pathol. 2012; 36:1691-1699.
7. Lagana S, et al. Utility of an immunohistochemical panel consisting of glypican-3, heat-shock protein-70, and glutamine synthetase in the distinction of low-grade hepatocellular carcinoma from hepatocellular adenoma. Appl Immunohistochem Mol Morphol. 2013; 21:170-76.
8. 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

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