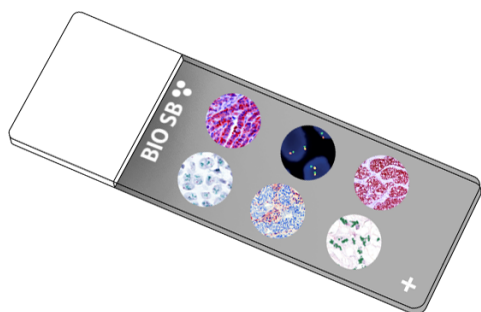


# HEG1

## Control Slides



### Intended Use

For In Vitro Diagnostic Use.

### Summary and Explanation

Sialylated protein HEG homolog 1 or Heart development protein with EGF like domains 1 (HEG1) is a novel calcium binding receptor protein involved in the Cerebral Cavernous Malformations pathway and plays a regulatory role in heart and vessel formation by stabilizing endothelial cell junctions. HEG1 is a heavily glycosylated protein that participates in endothelial cell associations that develop the vascular system, and therefore plays a role in angiogenesis and the microenvironment of cellular adhesion. The exact role of HEG1 in hepatocellular carcinoma is unclear, however, studies have shown HEG1 indicates poor prognosis and plays important roles in hepatocellular carcinoma invasion, metastasis, and epithelial mesenchymal transition by activating Wnt/ $\beta$ -catenin signaling. HEG1 mucin-like membrane protein has also been found to be a sensitive and specific biomarker for malignant mesothelioma in pleural (lung) and peritoneal (abdominal) membranes, and several other rare locations, where it supports the survival and proliferation of mesothelioma cells. HEG1 is potentially a useful prognostic biomarker and therapeutic target for malignant mesothelioma and hepatocellular, thyroid, and ovarian carcinomas. HEG1 has been found to be a highly specific and sensitive marker of epithelioid Malignant Mesothelioma and offers sensitivity comparable to conventional markers for Epithelioid Mesotheliomas, but provides considerably better specificity, such that the diagnosis of epithelioid mesothelioma versus NSCLC and potentially could be confirmed with a combination of HEG1 and a suitable broad spectrum carcinoma marker such as Claudin-4.

### Presentation

Five slides of HEG1 positive tissues, each mounted on Hydrophilic Plus Slides, provided in a plastic mailer.

<i>Catalog No.</i>	<i>Quantity</i>
BSB-9204-CS	5 slides
BSB-3728-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. HEG1 Gene.  
<https://www.genecards.org/cgi-bin/carddisp.pl?gene=HEG12>. Kleaveland B, et al. Regulation of cardiovascular development and integrity by the heart of glass-cerebral cavernous malformation protein pathway. Nat Med. 2009;15(2):169-76. doi:10.1038/nm.19183. Zhao YR, et al. HEG1 indicates poor prognosis and promotes hepatocellular carcinoma invasion, metastasis, and EMT by activating Wnt/ $\beta$ -catenin signaling. Clin Sci. 2019;133(14):1645-1662. doi:10.1042/CS201902254. Tsuji S, et al. HEG1 is a novel mucin-like membrane protein that serves as a diagnostic and therapeutic target for malignant mesothelioma. Sci Rep. 2017;7:45768. <https://doi.org/10.1038/srep45768>. Jaso JR, et al. HEG1 Is a Highly Specific and Sensitive Marker of Epithelioid Malignant Mesothelioma. Am J Surg Pathol. 2020;44(8):1143-1148. doi: 10.1097/PAS.0000000000001469.6. Matsuura, R. et al. Identification of mesothelioma specific sialylated epitope recognized with monoclonal antibody SKM9-2 in a mucin-like membrane protein HEG1. Scientific Reports. 2018; 8:14251 doi:10.1038/s41598-018-32534-87. 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.

### Symbol Key / Légende des symboles/Erläuterung der Symbole

<b>EC REP</b>	QAdvis EAR AB Ideon Science Park Scheelevägen 17 SE-223 70 Lund, Sweden	 Storage Temperature Limites de température Zulässiger Temperaturbereich	 Manufacturer Fabricant Hersteller	<b>REF</b>	Catalog Number Référence du catalogue Bestellnummer
<b>IVD</b>	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 jusqu'à Verwendbar bis	<b>LOT</b>	Lot Number Code du lot Chargenbezeichnung