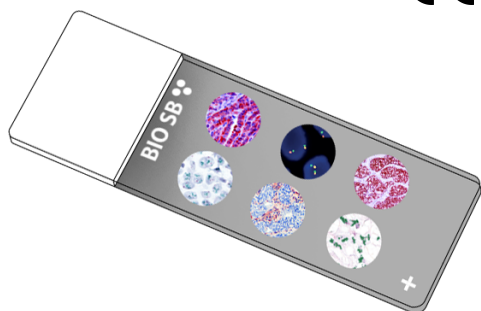


## HE4 Control Slides



### Intended Use

For In Vitro Diagnostic Use.

### Summary and Explanation

Human epididymis protein 4, also known as WAP four-disulfide core domain protein 2, is a protein that in humans is encoded by the WFDC2 gene. This gene encodes a protein that is a member of the WFDC domain family. The WFDC domain, or WAP Signature motif, functions as a protease inhibitor in many family members. The encoded protein is a small secretory protein, which may be involved in sperm maturation. HE4 gene expression has been found the highest in normal human trachea and salivary gland, and to a lesser extent, lung, prostate, pituitary gland, thyroid, and kidney. HE4 immunoreactivity has also been found in normal glandular epithelium of the female genital tract and breast, the epididymis and vas deferens, respiratory epithelium, distal renal tubules, colonic mucosa, and salivary glands which is consistent with the HE4 gene expression.

HE4 is a recognized biomarker in ovarian and endometrial cancer and over-expressed in pancreatic adenocarcinoma. In a series of 175 human adult tumors, gene expression was found to be the highest in ovarian serous carcinomas. However, adenocarcinomas of the lung, and occasional breast, transitional cell and pancreatic carcinomas had moderate or high levels of HE4 expression. IHC studies have shown that HE4 is significantly higher expressed in human pancreatic carcinoma tissues than in both normal and adjacent non-tumoral pancreatic tissues, and the staining intensity is inversely correlated with the clinical stage. HE4 is also highly expressed in early stage pancreatic adenocarcinoma.

### Presentation

Five slides of HE4 positive tissues, each mounted on Hydrophilic Plus Slides, provided in a plastic mailer.

<i>Catalog No.</i>	<i>Quantity</i>
BSB-9203-CS	5 slides
BSB 3355	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 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

1. Hellström I, et al. The HE4 (WFDC2) Protein Is a Biomarker for Ovarian Carcinoma. Cancer Research. 2003; 63 (13): 3695–3700.
2. Kirchhoff C, et al. A major human epididymis-specific cDNA encodes a protein with sequence homology to extracellular proteinase inhibitors. Biol Reprod. 1992; 45 (2): 350–7.
3. Schummer M, et al. Comparative hybridization of an array of 21,500 ovarian cDNAs for the discovery of genes overexpressed in ovarian carcinomas. Gene. 1999; 238 (2): 375–85.
4. Molina R, et al. HE4 a novel tumour marker for ovarian cancer: Comparison with CA 125 and ROMA algorithm in patients with gynaecological diseases. Tumor Biology. 2011; 32 (6): 1087–95.
5. Mary T Galgano, et al. Comprehensive analysis of HE4 expression in normal and malignant human tissues. Modern Pathology. 2006; 19, 847–853.
6. Tianhe Huang, et al. Expression and Diagnostic Value of HE4 in Pancreatic Adenocarcinoma. Int J Mol Sci. 2015 Feb; 16(2): 2956–2970.
7. 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

<b>EC</b> <b>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 jusque Verwendbar bis	<b>LOT</b>	Lot Number Code du lot Chargenbezeichnung