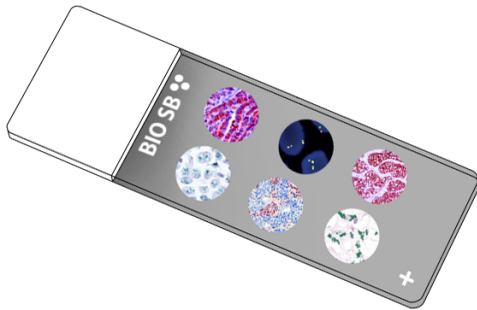


CD137/TNFRSF9

Control Slides



Intended Use

For In Vitro Diagnostic Use.

Summary and Explanation

CD137, or tumor necrosis factor receptor superfamily member 9, also known as 4-1BB, is encoded by the TNFRSF9 gene on chromosome 1p36.23. CD137/TNFRSF9 is expressed on the surface of certain immune cells, such as Follicular Dendritic Cells, Monocytes, Mast Cells and Granulocytes. CD137/TNFRSF9 is barely detected on resting T cells or T-cell lines, and expression of CD137 is therefore activation dependent. It is found on activated CD4+, CD8+ or Natural Killer Cells. Activation of CD137 by its ligand, CD137L, upregulates survival genes, enhances cell division, induces cytokine production, and prevents activation-induced cell death in T cells. One study demonstrated CD137/TNFRSF9 positive IHC staining in a majority of Classical Hodgkin Lymphoma (CHL) tissues, indicating its usefulness as a diagnostic biomarker for CHL. CD137/TNFRSF9 was also found to be a highly specific immunohistochemical marker of Neoplastic Follicular Dendritic Cells. Another study investigated CD137/TNFRSF9 via IHC in malignant tumor cells and found that there was an enhanced expression of CD137/TNFRSF9 in blood vessel cells of malignant tumors compared to blood vessel cells in benign tumors or inflammatory tissues. Further studies indicate the value of CD137/TNFRSF9 as a prognostic marker in Diffuse Large B-cell Lymphomas, tumor cell differentiation in Gastric Cancer as well as the correlation between CD137/TNFRSF9 expression and bone metastasis of Breast Cancer. CD137/TNFRSF9 is considerably up-regulated in human Gliomas when compared with normal brain tissue. In addition, data provides evidence for an immune cell-independent de novo expression pattern of CD137/TNFRSF9 in mainly non-neoplastic reactive astrocytes and excludes classic immunological cell types, namely lymphocytes and microglia as the source of CD137/TNFRSF9. Moreover, TNFRSF9 is predominantly expressed in a perivascular and peritumoral distribution with significantly higher expression in IDH-1 mutant gliomas.

Presentation

Five slides of CD137/TNFRSF9 positive tissues, each mounted on Hydrophilic Plus Slides, provided in a plastic mailer.

<i>Catalog No.</i>	<i>Quantity</i>
BSB-9066-CS	5 slides
BSB-3717-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 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. National Center for Biotechnology Information. TNFRSF9 TNF receptor superfamily member 9 [Homo sapiens (human)]. <https://www.ncbi.nlm.nih.gov/gene/3604.2>. Vinay DS, Kwon BS. Immunotherapy of cancer with 4-1BB. Mol Cancer Ther. 2012;11(5):1062-1070. doi:10.1158/1535-7163.MCT-11-06773. Glorieux C, Huang P. CD137 expression in cancer cells: regulation and significance. Cancer Commun (Lond). 2019;39(1):70. Published 2019 Nov 8. doi:10.1186/s40880-019-0419-z4. Anderson MW, Zhao S, Freud AG, et al. CD137 is expressed in follicular dendritic cell tumors and in classical Hodgkin and T-cell lymphomas: diagnostic and therapeutic implications. Am J Pathol. 2012;181(3):795-803. doi:10.1016/j.ajpath.2012.05.0155. Alizadeh AA, Gentles AJ, Alencar AJ, et al. Prediction of survival in diffuse large B-cell lymphoma based on the expression of 2 genes reflecting tumor and microenvironment. Blood. 2011;118(5):1350-1358. doi:10.1182/blood-2011-03-3452726. Jiang P, Gao W, Ma T, et al. CD137 promotes bone metastasis of breast cancer by enhancing the migration and osteoclast differentiation of monocytes/macrophages. Theranostics. 2019;9(10):2950-2966. Published 2019 May 9. doi:10.7150/thno.296177. Broll K, Richter G, Pauly S, Hofstaedter F, Schwarz H. CD137 expression in tumor vessel walls. High correlation with malignant tumors. Am J Clin Pathol. 2001;115(4):543-549. doi:10.1309/e343-kmyx-w3y2-10ky8. Hu BS, Tang T, Jia JL, et al. CD137 agonist induces gastric cancer cell apoptosis by enhancing the functions of CD8+ T cells via NF-κB signaling. Cancer Cell Int. 2020;20:513. Published 2020 Oct 20. doi:10.1186/s12935-020-01605-09. Blank AE, Baumgarten P, Zeiner P, et al. Tumour necrosis factor receptor superfamily member 9 (TNFRSF9) is up-regulated in reactive astrocytes in human gliomas. Neuropathol Appl Neurobiol. 2015;41(2):e56-e67. doi:10.1111/nan.1213510. 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	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