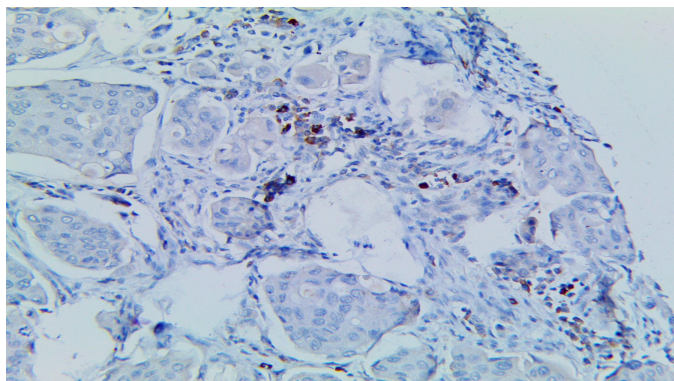


CD137/TNFRSF9

Clone: BSB-159
Mouse Monoclonal



Inset: IHC of CD137/TNFRSF9 on a FFPE Transitional Cell Carcinoma Tissue

Intended Use

For In Vitro Diagnostic Use.

This antibody is intended for use in Immunohistochemical applications on formalin-fixed paraffin-embedded tissues (FFPE), frozen tissue sections, and cell preparations. Interpretation of results should be performed by a qualified medical professional.

Immunogen

Synthetic peptide corresponding to the N-terminus of the human CD137 protein.

Summary and Explanation

CD137, or tumor necrosis factor receptor superfamily member 9 (TNFRSF9), 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.

Antibody Type	Mouse Monoclonal	Clone	BSB-159
Isotype	IgM	Reactivity	Paraffin, Frozen
Localization	Nuclear, Membranous	Species Reactivity	Human
Control	Colon, Stomach, Tonsil, Testis, Transitional Cell Carcinoma, DBC, Hepatocellular Carcinoma, Diffuse Type Gastric Carcinoma		
Application	Hodgkin's & Non Hodgkin's Lymphoma, Lymphoma, Leukemia & Histiocytic, Gastric Cancer, Breast Cancer & Infectious Disease		

Presentation

Anti-CD137/TNFRSF9 is a Mouse Monoclonal antibody derived from cell culture supernatant that is concentrated, dialyzed, filter sterilized and diluted in buffer pH 7.5, containing BSA and sodium azide as a preservative.

<i>Catalog No.</i>	<i>Presentation</i>	<i>Dilution</i>	<i>Volume</i>
BSB-3717-3	Predilute	Ready-to-Use	3.0 mL
BSB-3717-7	Predilute	Ready-to-Use	7.0 mL
BSB-3717-15	Predilute	Ready-to-Use	15.0 mL
BSB-3717-01	Concentrate	1:25-1:100	0.1 mL
BSB-3717-05	Concentrate	1:25-1:100	0.5 mL
BSB-3717-1	Concentrate	1:25-1:100	1.0 mL

Control Slides Available

<i>Catalog No.</i>	<i>Quantity</i>
BSB-9066-CS	5 slides

Storage Store at 2-8°C (Control Slides: Store at 20-25°C)

Precautions

1. For professional users only. Results should be interpreted by a qualified medical professional.
2. This product contains <0.1% sodium azide (NaN₃) as a preservative. 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. Do not ingest reagent. If reagent is ingested, seek medical advice immediately.
6. Avoid contact with eyes. If contact occurs, flush with large quantities of water.
7. 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".

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. Temperature fluctuations should be avoided. Store appropriately when not in use, and avoid prolonged exposure to room temperature.

Specimen Preparation

Paraffin sections: The antibody can be used on formalin-fixed paraffin-embedded (FFPE) tissue sections. Ensure tissue undergoes appropriate fixation for best results. Pre-treatment of tissues with heat-induced epitope retrieval (HIER) is recommended using Bio SB ImmunoDNA Retriever with Citrate (BSB 0020-BSB 0023), ImmunoDNA Retriever with EDTA (BSB 0030-BSB 0033), or ImmunoDNA Digestor (BSB 0108-0112). See reverse side for complete protocol. Tissue should remain hydrated via use of Bio SB Immuno/DNA Washer solutions (BSB 0029 & BSB 0042).

Frozen sections and cell preparations: The antibody can be used on acetone-fixed frozen sections and acetone-fixed cell preparations.

IHC Protocol

1. Cut and mount 3-5 micron formalin-fixed paraffin-embedded tissues on positively charged slides such as Bio SB Hydrophilic Plus Slides (BSB 7028).
2. Air dry for 2 hours at 58° C.
3. Deparaffinize, dehydrate and rehydrate tissues.
4. 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).
5. 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.
6. After heat treatment, transfer slides in ImmunoDNA Retriever with Citrate or EDTA to room temperature and let stand for 15-20 minutes.
 7. For manual IHC, perform antibody incubation at ambient temperature. For automated IHC methods, perform antibody incubation according to instrument manufacturer's instructions.
 8. Wash slides with ImmunoDNA washer or DI water.
 9. Continue IHC 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

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.

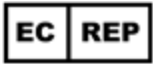







Product Limitations

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-11-0677
3. 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-z
4. 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.2012.05.015
5. 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-2011-03-345272
6. 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.29617
7. 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-w3y2-10ky
8. 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/s12935-020-01605-0
9. 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.12135
10. 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

	EMERGO EUROPE Prinsessegracht 20 2514 AP The Hague The Netherlands		Storage Temperature Limites de température Zulässiger Temperaturbereich		Manufacturer Fabricant Hersteller		Catalog Number Référence du catalogue Bestellnummer
	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 Number Code du lot Chargenbezeichnung