

INSM1 (A-8)


Mouse anti-human INSM1 (Insulinoma-associated protein 1) Monoclonal Antibody (Clone A-8)

REFERENCES AND PRESENTATIONS¹

- **ready-to-use (manual or LabVision AutoStainer)**
MAD-000777QD-3
MAD-000777QD-7
MAD-000777QD-12
- **Ready-to-use (MD-Stainer)²**
MAD-000777QD-3/V
MAD-000777QD/V
- **concentrated**
MAD-000777Q - 1:100 recommended dilution

COMPOSITION:

Anti-human INSM1 mouse monoclonal antibody purified from serum and prepared in 10mM PBS, pH 7.4, with 0.2% BSA and 0.09% sodium azide

INTENDED USE : Immunohistochemistry (IHC) on paraffin embedded tissues. Not tested on frozen tissues or Western-Blotting

CLONE: A-8

ISOTYPE: Mouse IgG1/kappa

SPECIES REACTIVITY: In vitro diagnostics in humans. Not tested in other species

DESCRIPTION AND APPLICATIONS:

INSM1 protein, also known as IA1, is a nuclear transcription factor encoded by INSM1 gene, located in the chromosome region 20p11.23 and composed of 510 amino acids with a molecular mass of approximately 52.8kDa. The protein, which shows a wide homology in different species, contains a C-terminal portion with 5 finger-binding domains and an N-terminal domain with four pro-hormone conversion sites as well as an amidation signal sequence.

INSM1 factor plays an important role in neurogenesis and differentiation during the embryonic and fetal development of the pancreatic neuroendocrine, anterior pituitary, intestine cells and synapto-adrenal cells of the peripheral nervous system. INSM1 gene, which does not express in normal endocrine and non-

endocrine tissues in adults, acts as a suppressor gene of the transmission pathways NEUROD1 and INS after interaction with Cyclin D1, inhibits the specific genes of the skeletal muscle in neuroendocrine cells of the pituitary and suppress neural factors such as HDAC1, HDAC2, HDAC3 and KDM1A (involved in the incorporation of chromatin-modifying factors). In addition to this, it suppresses the activity of the histone deacetylase RCOR1.

Although normal endocrine tissues in adults do not show staining with INSM1, the marker is positive in neuroendocrine tumors including pheochromocytoma, medullary thyroid cancer, insulinoma, pituitary tumors and small-cell lung carcinoma, which show staining in the vast majority of the cases.

Especially in thoracic neuroendocrine tumors, the marker INSM1 shows higher specificity and sensitivity than Synaptophysin, Chromogranin and/or CD56, with the antibody marking approximately 95% of small-cell carcinomas and 91% of large-cell neuroendocrine carcinomas. All atypical and typical carcinoid tumors as well as mediastinal paragangliomas have been positive, which makes it a useful marker in differential diagnosis with other lung lesions, since only 3% of adenocarcinomas and slightly over 4% of squamous carcinomas can be positive. The high sensitivity and specificity of the antibody in lung lesions recommends the antibody as the only neuroendocrine marker, which allows better management of the scarce biopsical material. However, some studies report higher sensitivity of the combination of CD56 and Synaptophysin in the diagnosis of large-cell neuroendocrine carcinomas.

In small-cell prostate carcinoma, staining is higher in over 90% of the cases in contrast to usual markers both in primary tumors and metastases.

In brain tumors, despite the negativeness in adult parenchyma including gliosis areas, INSM1 has shown staining in almost 90% of medulloblastomas and in all central neurocytomas and pituitary adenomas. Patched staining has been described in embryonal tumors and high-grade gliomas.

Finally, a high specificity and sensitivity has been obtained in neuroendocrine tumors of the head and neck (middle ear adenoma, olfactory neuroblastoma and sinonasal teratocarcinoma, among others), neuroendocrine tumors of the uterine cervix and Merkel-cell carcinomas.

¹ These references are for presentation in vials of Low Density Polyethylene (LDPE) dropper. In case the products are used in automated stainers, a special reference is assigned as follows:

- / L: Cylindrical screw-cap vials (QD-3 / L, QD-7 / L, QD-12 / L).

- / N: Polygonal screw-cap vials (QD-3 / N, QD-7 / N, QD-12 / N).

For different presentations (references / volumes) please contact the supplier.

² For Technical specifications for MD-Stainer, please contact your distributor.



Vitro S.A.

Calle Luís Fuentes Bejarano 60 Ed. Nudo Norte Local 3 41020 Sevilla (Spain)

Tel: +34 954 933 200. vitr@vitro.bio; www.vitro.bio





2020-09-21

IHC POSITIVE CONTROL: Section from Merkel-cell carcinoma, small-cell lung carcinoma.

VISUALIZATION: Nuclear

IHC RECOMMENDED PROCEDURE:

- 4µm thick section should be taken on charged slides; dry overnight at 60°C
- Deparaffinise, rehydrate and HIER (heat induced epitope retrieval) – boil tissue in the Pt Module using Vitro S.A CITRATE buffer pH6³ for 20 min at 95°C. Upon completion rinse with 3-5 changes of distilled or deionised water followed by cooling at RT for 20 min
- Endogenous peroxidase block - Blocking for 10 minutes at room temperature using peroxidase solution (ref. MAD-021540Q-125)
- Primary antibody: incubate for 20 minutes [The antibody dilution (when concentrated) and protocol may vary depending on the specimen preparation and specific application. Optimal conditions should be determined by the individual laboratory]
- For detection use Master Polymer Plus Detection System (HRP) (DAB included; ref. MAD-000237QK)
- Counterstaining with haematoxylin and final mounting of the slide

STORAGE AND STABILITY:  Stored at 2-8°C. Do not freeze.  Once the packaging has been opened it can be stored until the expiration date of the reagent indicated on the label. If the reagent has been stored under other conditions to those indicated in this document, the user must first check its correct performance taking into account the product warranty is no longer valid.

WARNINGS AND PRECAUTIONS:

1. Avoid contact of reagents with eyes and mucous membranes. If reagents come into contact with sensitive areas, wash with copious amounts of water.
2. This product is harmful if swallowed.
3. Consult local or state authorities with regard to recommended method of disposal.
4. Avoid microbial contamination of reagents.

SAFETY RECOMMENDATIONS:

This product is intended for laboratory professional use only. The product is NOT intended to be used as a drug or for domestic purposes. The current version of the Safety Data Sheet for this product can be downloaded by searching the reference number at www.vitro.bio or can be requested at regulatory@vitro.bio.

³ Ref: MAD-004071R/D



BIBLIOGRAPHY:










1. Goto Y, De Silva MG, Toscani A, Prabhakar BS, Notkins AL, Lan MS. A novel human insulinoma-associated cDNA, IA-1, encodes a protein with "zinc-finger" DNA-binding motifs. *J Biol Chem.* 1992 Jul 25;267(21):15252-7.
2. Breslin MB, Zhu M, Lan MS. NeuroD1/E47 regulates the E-box element of a novel zinc finger transcription factor, IA-1, in developing nervous system. *J Biol Chem.* 2003 Oct 3;278(40):38991-7
3. Liu WD, Wang HW, Muguira M, Breslin MB, Lan MS. INSM1 functions as a transcriptional repressor of the neuroD/beta2 gene through the recruitment of cyclin D1 and histone deacetylases. *Biochem J.* 2006 Jul 1;397(1):169-77.
4. Mellitzer G, Bonn  S, Luco RF, Van De Castele M, Lenne-Samuel N, Collombat P, Mansouri A, Lee J, Lan M, Pipeleers D, Nielsen FC, Ferrer J, Gradwohl G, Heimberg H. IA1 is NGN3-dependent and essential for differentiation of the endocrine pancreas. *EMBO J.* 2006 Mar 22;25(6):1344-52.
5. Zhang T, Liu WD, Saunee NA, Breslin MB, Lan MS. Zinc finger transcription factor INSM1 interrupts cyclin D1 and CDK4 binding and induces cell cycle arrest. *J Biol Chem.* 2009 Feb 27;284(9):5574-81.
6. Lan MS, Breslin MB. Structure, expression, and biological function of INSM1 transcription factor in neuroendocrine differentiation. *FASEB J.* 2009 Jul;23(7):2024-33.
7. Xin Z, Zhang Y, Jiang Z, Zhao L, Fan L, Wang Y, Xie S, Shanguan X, Zhu Y, Pan J, Liu Q, Huang Y, Dong B, Xue W. Insulinoma-associated protein 1 is a novel sensitive and specific marker for small cell carcinoma of the prostate. *Hum Pathol.* 2018 Sep;79:151-159.
8. Ames HM, Rooper LM, Lattera JJ, Eberhart CG, Rodriguez FJ. INSM1 Expression Is Frequent in Primary Central Nervous System Neoplasms but Not in the Adult Brain Parenchyma. *J Neuropathol Exp Neurol.* 2018 May 1;77(5):374-382.
9. Rooper LM, Sharma R, Li QK, Illei PB, Westra WH. INSM1 Demonstrates Superior Performance to the Individual and Combined Use of Synaptophysin, Chromogranin and CD56 for Diagnosing Neuroendocrine Tumors of the Thoracic Cavity. *Am J Surg Pathol.* 2017 Nov;41(11):1561-1569.
10. Mukhopadhyay S, Dermawan JK, Lanigan CP, Farver CF. Insulinoma-associated protein 1

(INSM1) is a sensitive and highly specific marker of neuroendocrine differentiation in primary lung neoplasms: an immunohistochemical study of 345 cases, including 292 whole-tissue sections. Mod Pathol. 2018 Aug 28. doi: 10.1038/s41379-018-0122-7. [Epub ahead of print]

11. Kriegsmann K, Zgorzelski C, Kazdal D, Cremer M, Muley T, Winter H, Longuespée R, Kriegsmann J, Warth A, Kriegsmann M. Insulinoma-associated Protein 1 (INSM1) in Thoracic Tumors is Less Sensitive but More Specific Compared With Synaptophysin, Chromogranin A, and CD56. Appl Immunohistochem Mol Morphol. 2018 Oct 24. doi: 10.1097/PAI.0000000000000715. [Epub ahead of print]
12. Rooper LM, Bishop JA, Westra WH. INSM1 is a Sensitive and Specific Marker of Neuroendocrine Differentiation in Head and Neck Tumors. Am J Surg Pathol. 2018 May;42(5):665-671.
13. Kuji S, Watanabe R, Sato Y, Iwata T, Hirashima Y, Takekuma M, Ito I, Abe M, Nagashio R, Omae K, Aoki D, Kameya T. A new marker, insulinoma-associated protein 1 (INSM1), for high-grade neuroendocrine carcinoma of the uterine cervix: Analysis of 37 cases. Gynecol Oncol. 2017 Feb;144(2):384-390.
14. Rush PS, Rosenbaum JN, Roy M, Baus RM, Bennett DD, Lloyd RV. Insulinoma-associated 1: A novel nuclear marker in Merkel cell carcinoma (cutaneous neuroendocrine carcinoma). J Cutan Pathol. 2018 Feb;45(2):129-135.

LABEL AND BOX SYMBOLS

Explanation of the symbols of the product label and box:

	Expiration date
	Temperature limit
	Manufacturer
	Sufficient content for <n> assays
	Catalog number
	Lot code
	Refer to the instructions of use
	Medical product for <i>in vitro</i> diagnosis.
	Material safety data sheet