

SMAD4/Dpc4

Mouse Anti-Human SMAD4/Dpc4 Monoclonal Antibody (Clone B8)

References and presentations¹

- **ready-to-use** (manual or LabVision AutoStainer)
MAD-000792QD-3
MAD-000792QD-7
MAD-000792QD-12
- **Ready-to-use (MD-Stainer)²**
MAD-000792QD-3/V
MAD-000792QD/V
- **concentrated**
MAD-000792Q - 1:50 recommended dilution

Composition: Anti-human SMAD4/Dpc4 mouse monoclonal antibody obtained from ascitic fluid and prepared in 10mM PBS, pH 7.4, with 0.2% BSA and 0.09% sodium azide.

Intended use^{IVD}: Immunohistochemistry (IHC) on paraffin embedded tissues. Not tested on frozen tissues or Western-Blotting

Clone: B8

Ig isotype: Mouse IgG1/K

Immunogen: N/A

Species reactivity: In vitro diagnostics in humans. Not tested in other species

Description and applications:

The Mothers Against Decapentaplegic homolog 4 (SMAD4) protein, also known as MADH4, MAN-related protein 4, MAD, pancreatic carcinoma deletion factor 4 or DPC4, is linked to the SMAD4 suppressor gene, which consists of 11 exons, and is located in the genomic region 18q21.1. This gene shows allelic or biallelic loss in 50% of pancreatic carcinomas.

The SMAD4 protein, which is approximately 85% similar to the Mad proteins of *Drosophila* or sma 2,3 and 4 of *Caenorhabditis elegans*, is part of a nuclear heterodimeric complex consisting of SMAD2, 3 and 4 as well as the multimeric SMAD3/SMAD4/JUN/FOS

complex. Both complexes are involved in the transcription and signaling of the transforming growth factor beta (TGF beta) family, a group of cytokines that play important roles in embryonic development, tissue homeostasis and regeneration, and tissue regeneration and regulation of the immune system. TGF beta receptor activation is in turn promoted by that of SMAD2 and SMAD3 and simultaneously triggers the interaction of both with SMAD4. This process is necessary for the resulting heterodimer to penetrate the nucleus and to trigger cell signaling mechanisms linked to JUN/FOS. For this reason, the activated SMAD4 protein is the most frequently related one to the transcription of the TGF beta and BMP signaling pathways, being responsible, among many other functions, for the balance between muscle atrophy and hypertrophy.

In pathology, approximately 55% of invasive ductal carcinomas of the pancreas and adenocarcinomas of the extrahepatic bile ducts lose nuclear and cytoplasmic expression of SMAD4, 35% of them in associated with heterozygous deletions (of one allele) and 20% with homozygous deletions (of both alleles) of the gene. As the loss of expression of this gene has also been observed in pancreatic ductal neoplasms in situ, caution should be exercised in the interpretation of the loss of SMAD4 immunostaining, which should always be evaluated together with the histological features of the tumor.

In in situ papillary mucinous pancreatic tumors, if the loss of SMAD4 is associated with that of p16 protein, it may be indicative of progression of the tumor in situ towards invasive lesions. Moreover, it should be mentioned that some isolated cases of primary or metastatic neuroendocrine neoplasia of the pancreas also present loss of SMAD4 expression, suggesting the existence of new carcinogenesis pathways for these tumors.

In colorectal carcinomas with a stable microsatellite phenotype and in advanced stages of dysplasia in colonic adenomas, both with deletion of genetic material in chromosomal region 18q, loss of SMAD4 protein expression can be observed in approximately 40% of cases. On the contrary, if the microsatellite phenotype is unstable, only a percentage of less than 5% can present negativity for this marker.

Other genetic diseases and tumors with SMAD4 mutations and negativity of its protein expression,

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.

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and for which this antibody may be useful, are juvenile polyposis syndrome associated or not with hereditary hemorrhagic telangiectasia and ovarian, breast or prostate carcinomas.

IHC positive control: Tissue section from ductal carcinoma of the pancreas.

Visualization: Loss of staining in tissue with mutation; staining of membrane and cytoplasm in tissues without mutation.

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 EDTA buffer pH8³ 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.

BIBLIOGRAPHY

1. Hahn SA, Schutte M, Hoque AT, Moskaluk CA, da Costa LT, Rozenblum E, Weinstein CL, Fischer A, Yeo CJ, Hruban RH, Kern SE. DPC4, a candidate tumor suppressor gene at human chromosome 18q21.1. Science. 1996 Jan 19;271(5247):350-3.
2. Davis BN, Hilyard AC, Lagna G, Hata A. SMAD proteins control DROSHA-mediated microRNA maturation. Nature. 2008 Jul 3;454(7200):56-61.
3. Massagué, Joan (2012). TGFβ signalling in context. Nature Reviews Molecular Cell Biology. 13 (10): 616–630.
4. Hahn SA, Schutte M, Hoque AT, Moskaluk CA, da Costa LT, Rozenblum E, Weinstein CL, Fischer A, Yeo CJ, Hruban RH, Kern SE. DPC4, a candidate tumor suppressor gene at human chromosome 18q21.1. Science. 1996 Jan 19;271(5247):350-3.
5. Howe JR, Roth S, Ringold JC, Summers RW, Järvinen HJ, Sistonen P, Tomlinson IP, Houlston RS, Bevan S, Mitros FA, Stone EM, Aaltonen LA. Mutations in the SMAD4/DPC4 gene in juvenile polyposis. Science. 1998 May 15;280(5366):1086-8.
6. Zhou S, Buckhaults P, Zawel L, Bunz F, Riggins G, Dai JL, Kern SE, Kinzler KW, Vogelstein B. Targeted deletion of Smad4 shows it is required for transforming growth factor beta and activin signaling in colorectal cancer cells. Proc Natl Acad Sci U S A. 1998 Mar 3;95(5):2412-6
7. Scarpa A, Orlandini S, Moore PS, Lemoine NR, Beghelli S, Baron A, Falconi M, Zamboni G. Dpc4 is expressed in virtually all primary and metastatic pancreatic endocrine carcinomas. Virchows Arch. 2002 Feb;440(2):155-159
8. Wilentz RE, Su GH, Dai JL, Sparks AB, Argani P, Sohn TA, Yeo CJ, Kern SE, Hruban RH. Immunohistochemical labeling for dpc4 mirrors genetic status in pancreatic adenocarcinomas : a new marker of DPC4 inactivation. Am J Pathol. 2000 Jan;156(1):37-43
9. Tascilar M, Offerhaus GJ, Altink R, Argani P, Sohn TA, Yeo CJ, Cameron JL, Goggins M, Hruban RH, Wilentz RE.

3 Ref: MAD-004072R/D



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Immunohistochemical labeling for the Dpc4 gene product is a specific marker for adenocarcinoma in biopsy specimens of the pancreas and bile duct. Am J Clin Pathol. 2001 Dec;116(6):831-7

10. Biankin AV, Biankin SA, Kench JG, Morey AL, Lee CS, Head DR, Eckstein RP, Hugh TB, Henshall SM, Sutherland RL. Aberrant p16(INK4A) and DPC4/Smad4 expression in intraductal papillary mucinous tumours of the pancreas is associated with invasive ductal adenocarcinoma. Gut. 2002 Jun;50(6):861-8
11. Salovaara R, Roth S, Loukola A, Launonen V, Sistonen P, Avizienyte E, Kristo P, Järvinen H, Souchelnytskyi S, Sarlomo-Rikala M, Aaltonen LA. Frequent loss of SMAD4/DPC4 protein in colorectal cancers. Gut. 2002 Jul;51(1):56-9
12. Isaksson-Mettävainio M, Palmqvist R, Forsell J, Stenling R, Oberg A. SMAD4/DPC4 expression and prognosis in human colorectal cancer. Anticancer Res. 2006 Jan-Feb;26(1B):507-10

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

