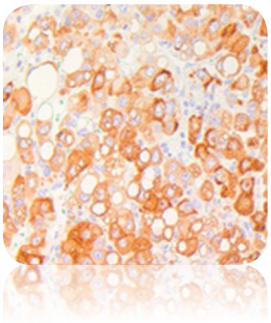
New Antibodies for Immunohistochemistry 2019

Volume 1

medac

New Antibodies from medac Portfolio

ACSL4 (Acyl-CoA Synthetase Long Chain Family Member 4) (EP386), *rabbit monoclonal*



- 0.1 ml concentrate . . . . . #AC-0345RUO
- 1.0 ml concentrate . . . . . #AC-0345RUOC

The Acyl-CoA Synthetase Long Chain Family Member 4 (ACSL4) is an essential fatty acid synthetase and its mRNA is highly expressed in placenta, brain, testis, ovary, spleen and adrenal gland. Intracellularly, ACSL4 is localized in the cytoplasm with peroxisomes and mitochondria. Altered expression of lipid metabolic enzymes is a feature of a variety of cancers. ACSL4 was reported to be inversely correlated with sex steroid receptor (ER and AR) expression in breast and prostate carcinomas. The inverse correlation was indicative of resistance to hormone-based treatment in these tumors.

Literature:

1. Wu X, et al. Long chain fatty Acyl-CoA synthetase 4 is a biomarker for and mediator of hormone resistance in human breast cancer. PLoS One. 2013; 8(10): e77060.
2. Creighton J, et al. Expression of Long-chain Fatty Acyl-CoA Synthetase 4 in Breast and Prostate Cancers Is Associated with Sex Steroid Hormone Receptor Negativity. Translational Oncology 2010; 3(2): 91-98.
3. Wu X, et al. ACSL4 promotes prostate cancer growth, invasion and hormonal resistance. Oncotarget. 2015; 6(42): 44849–44863.

ARD1 (ADP-ribosylation factor domain protein 1) (EP357), *rabbit monoclonal*

- 0.1 ml concentrate . . . . . #AC-0343RUO
- 1.0 ml concentrate . . . . . #AC-0343RUOC

Arrest-defect-1 protein (ARD1) is the catalytic subunit of NatA acetyltransferase responsible for N-terminal alpha-acetylation. ARD1 is present in the cytoplasm and nucleus, and is also required for cellular proliferation. Its role in tumorigenesis is under debate. ARD1 was reported to have both oncogenic and tumor suppressor function.

Literature:
1. DePaolo JS, et al. Acetylation of androgen receptor by ARD1 promotes dissociation from HSP90 complex and prostate tumorigenesis. Oncotarget. 2016; 7(44): 71417-71428.
2. Kuo HP, et al. Arrest-defective-1 protein (ARD1): tumor suppressor or oncoprotein? Am J Transl Res. 2010; 2(1):56-64.
3. Lim JH, et al. Human arrest defective 1 acetylates and activates beta-catenin, promoting lung cancer cell proliferation. Cancer Res. 2006; 66(22): 10677-82.
4. Wang ZH, et al. Up-regulation of human arrest-defective 1 protein is correlated with metastatic phenotype and poor prognosis in breast cancer. Asian Pac J Cancer Prev. 2011; 12(8): 1973-7.

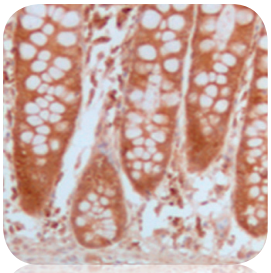
ATM (Ataxia Telangiectasia Mutated) (EP327), *rabbit monoclonal*

- 0.1 ml concentrate . . . . . #AC-0287RUO
- 1.0 ml concentrate . . . . . #AC-0287RUOC

ATM (ataxia-telangiectasia mutated) is a serine/threonine protein kinase responsible for regulating the cell cycle checkpoint. It is predominantly localized in the nucleus, associated with chromatin and nuclear matrix. ATM is recruited to sites of DNA double-strand breaks and is activated by autophosphorylation, where it functions as a tumor suppressor. Mutations in ATM were initially identified in the genetic disorder ataxia-telangiectasia, but deficiencies in ATM function are also reported in multiple tumor types, including cancers of the colon, breast, gastric, lung, and lymphoid tissues. Deficient ATM expression was associated with advanced stages of cancer, and correlated with shorter disease-free and overall survival rates.

Literature:
1. Cremona CA, Behrens A. ATM signalling and cancer. Oncogene 2014; 33: 3351–3360.
2. Petersen LF, et al. Loss of tumour-specific ATM protein expression is an independent prognostic factor in early resected NSCLC. Oncotarget. 2017; 8(24): 38326-38336.
3. Suh KJ, et al. Loss of ataxia-telangiectasia-mutated protein expression correlates with poor prognosis but benefits from anthracycline-containing adjuvant chemotherapy in breast cancer. Breast Cancer Res Treat. 2016; 158(2): 233-41.

BAD (Bcl-2-Antagonist of Cell Death) (EP315), *rabbit monoclonal*

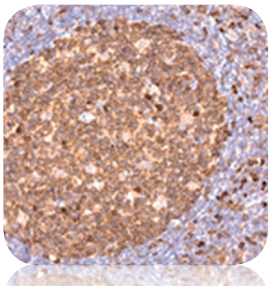


- 0.1 ml concentrate . . . . . #AC-0288RUO
- 1.0 ml concentrate . . . . . #AC-0288RUOC

BAD (Bcl-2-Antagonist of Cell Death) is a pro-apoptotic member of the Bcl-2 family which interacts with Bcl-2 and Bcl-XL. BAD is localized in the cytoplasm and is activated upon dephosphorylation. It is broadly expressed in human tissues, including the skin, heart, lung, stomach, colon, liver, kidney, and pancreas. Loss of BAD protein has been reported to contribute to tumorigenesis and chemotherapy resistance. BAD expression has been studied in prostate cancer, non-small cell lung carcinoma (NSCLC), and hepatocellular carcinomas. Decreased BAD expression was reported in 50% of hepatocellular carcinomas, and loss of BAD was shown to be an independent marker of poor prognosis in NSCLC patients.

Literature:
1. Galmiche A, et al. BAD, a proapoptotic member of the BCL2 family, is a potential therapeutic target in hepatocellular carcinoma. Mol Cancer Res. 2010; 8(8): 1116-25.
2. Jiang L, et al. BAD overexpression inhibits cell growth and induces apoptosis via mitochondrial-dependent pathway in non-small cell lung cancer. Cancer Cell Int. 2013; 13(1): 53.
3. Smith AJ, et al. Expression of the Bcl-2 protein BAD promotes prostate cancer growth. PLoS One. 2009 13; 4(7): e6224.

Caspase-3 (CPP32) (EP410), *rabbit monoclonal*

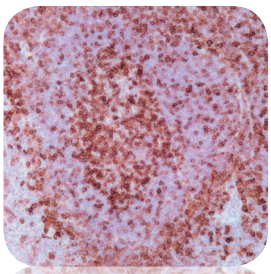


- 0.1 ml concentrate . . . . . #AC-0364RUO
- 1.0 ml concentrate . . . . . #AC-0364RUOC

Caspase-3 is a protease with a central role in the execution phase of cellular apoptosis. It is initially synthesized as procaspase-3. Upon cleavage by initiator caspases, an active heterotetrameter is formed composing of large (p17) and small (p12) caspase-3 subunits. Although the precursor form of caspase-3 is localized in the cytoplasm, activated caspase-3 undergo nuclear translocation. Clone EP410 detects both procaspase-3 and cleaved caspase-3 forms. Capase-3 expression is detected in both, the nucleus and cytoplasm of tumor cells. Caspase-3 expression was already investigated in non-small cell lung carcinoma, breast and colorectal cancer but its prognostic utility is controversial.

Literature:
1. Hu Q, et al. Elevated cleaved caspase-3 is associated with shortened overall survival in several cancer types. Int J Clin Exp Pathol. 2014; 7(8): 5057-70.
2. Nassar A; et al. Survivin and caspase-3 expression in breast cancer: correlation with prognostic parameters, proliferation, angiogenesis, and outcome. Appl Immunohistochem Mol Morphol. 2008 Mar; 16(2): 113-20.
3. Persad R, et al. Overexpression of caspase-3 in hepatocellular carcinomas. Mod Pathol. 2004; 17(7): 861-7.

CD27 (EPR8569), *rabbit monoclonal*

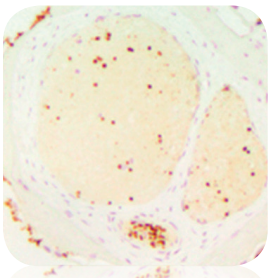


- 3.0 ml ready to use #MAD-000762Q-3
- 7.0 ml ready to use #MAD-000762Q-7
- 12.0 ml ready to use #MAD-000762Q-12

CD27 is a member of the TNF-receptor superfamily and is relevant for checkpoint-regulation. It is expressed on the majority of T cells, some NK cells and memory B cells. Through interaction with its ligand CD70, CD27 transduces a co-stimulatory signal promoting T cell and NK cell activation and cytotoxicity. Recent studies have shown that modulating the CD70-CD27 interaction is an attractive strategy to treat solid tumors and also to directly target leukemia stem cells.

Literature:
1. Borst J, et al. CD27 and CD70 in T cell and B cell activation. Curr Opin Immunol. 2005; 17(3): 275-81.
2. Riether C, et al. Modulating CD27 signaling to treat cancer. Oncoimmunology. 2012; 1(9): 1604–1606.

CD42b (EP409), *rabbit monoclonal*

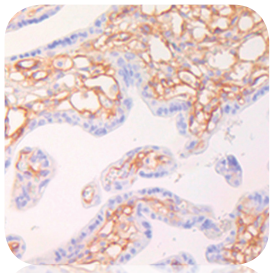


- 0.1 ml concentrate . . . . . #AC-0336A
- 1.0 ml concentrate . . . . . #AC-0336

CD42b, encoded by the GP1BA gene, is a surface membrane glycoprotein expressed on the membrane of megakaryocytes, splenocytes and platelets. CD42b forms a part of the CD42a-d complex (also called the glycoprotein Ib-IX-V receptor) and is the surface platelet receptor for von Willebrand factor (vWF) on endothelium. CD42b is useful in differentiating acute megakaryoblastic leukemia subtype M7 (AML-M7) that are typically positive for CD41, CD42b and CD61 from acute myelofibrosis, which are CD42b negative.

Literature:
1. Inaba H, et al. Heterogeneous cytogenetic subgroups and outcomes in childhood acute megakaryoblastic leukemia: a retrospective international studyBlood. 2015; 126(13): 1575-84.
2. Orazi A, et al. Acute panmyelosis with myelofibrosis: an entity distinct from acute megakaryoblastic leukemia. Mod Pathol. 2005; 18(5): 603-14.
3. Orazi A, et al. Chronic myelomonocytic leukemia: The role of bone marrow biopsy immunohistology. Mod Pathol. 2006; 19(12): 1536-45.
4. Toretsky JA, et al. Novel translocation in acute megakaryoblastic leukemia (AML-M7). J Pediatr Hematol Oncol. 2003; 25(5): 396-402.
5. Sun, T. (2009). Atlas of Hematologic Neoplasms. Springer Science & Business Media.

CD248 (Endosialin) (EP383), *rabbit monoclonal*

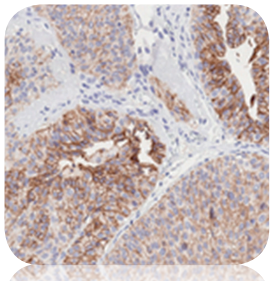


- 0.1 ml concentrate . . . . . #AC-0349A
- 1.0 ml concentrate . . . . . #AC-0349

CD248, known also as endosialin and tumor endothelial marker 1 (TEM1), is a 95-kDa transmembrane glycoprotein expressed in activated stromal and perivascular fibroblasts and pericytes. CD248 is an important regulator of critical pathways involved with stromal fibroblast migration, and proliferation. During normal embryonic development, CD248 is highly expressed across diverse tissue types. Postnatally, its expression is restricted to the endometrium, bone marrow and corpus luteum. CD248 is expressed within the endothelium across many tumor types include sarcomas, carcinoma and neuroectodermal tumors. Within the tumor stroma, activated fibroblasts subpopulations are often associated with poor prognosis.

Literature:
1. Bagley RG, et al. Human endothelial precursor cells express tumor endothelial marker 1/endosialin/CD248. Mol Cancer Ther. 2008; 7(8): 2536-46.
2. Hardie DL, et al. The stromal cell antigen CD248 (endosialin) is expressed on naive CD8+ human T cells and regulates proliferation. Immunology. 2011; 133(3): 288-95.
3. Maia M, et al. CD248 facilitates tumor growth via its cytoplasmic domain. BMC Cancer. 2011; 11: 162.
4. Rettig WJ, et al. Identification of endosialin, a cell surface glycoprotein of vascular endothelial cells in human cancer. Proc Natl Acad Sci U S A. 1992; 89(22): 10832-6.

Claudin 4 (EP417), *rabbit monoclonal*

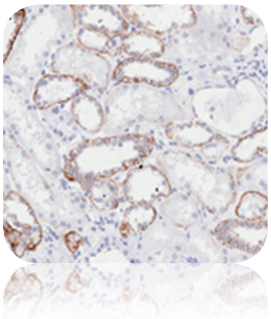


- 0.1 ml concentrate . . . . . #AC-0352A
- 1.0 ml concentrate . . . . . #AC-0352

Claudin-4 is one of twenty-seven integral membrane tight junction proteins and specialized in paracellular sodium transport. Claudin-4 is detectable in low amounts in the normal tissues of the lung, kidney, breast, prostate, bladder and gastrointestinal tract. It is a highly specific and sensitive membranous marker for most epithelial neoplasms. Absence of expression in normal mesothelium and mesothelioma provides utility in the differential diagnosis between carcinoma from mesothelioma. In breast tumors, claudin-4 levels are significantly higher in ER-negative and high grade tumors when compared to ER-positive and low grade tumors. High levels of Claudin-4 expression are associated with later stages of progression and reduced patient survival for most types of epithelial neoplasms. Conversely, its expression is downregulated in gastric and high-grade bladder cancers, and is significantly lower in lymph node metastasis and esophageal tumors with distant metastasis.

Literature:
1. Facchetti, F, et al. Claudin 4 identifies a wide spectrum of epithelial neoplasms and represents a very useful marker for carcinoma versus mesothelioma diagnosis in pleural and peritoneal biopsies and effusions. Virchows Arch. 2007; 451(3): 669-80.
2. Lonardi S, et al. Usefulness of Claudin 4 in the cytological diagnosis of serosal effusions. Diagn Cytopathol. 2011; 39(5): 313-7.
3. Schaefer IM, et al. Claudin-4 expression distinguishes SWI/SNF complex-deficient undifferentiated carcinomas from sarcomas. Mod Pathol. 2017; 30(4): 539-548.
4. Nichols LS, et al. Claudin 4 protein expression in primary and metastatic pancreatic cancer: support for use as a therapeutic target. Am J Clin Pathol. 2004; 121(2): 226-30.
5. Pan XY, et al. Expression of claudin-3 and claudin-4 in normal, hyperplastic, and malignant endometrial tissue. Int J Gynecol Cancer. 2007; 17(1): 233-41.

Claudin 7 (EP399), *rabbit monoclonal*

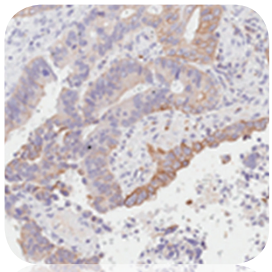


- 0.1 ml concentrate . . . . . #AC-0365A
- 1.0 ml concentrate . . . . . #AC-0365

Claudin 7 is a tight junction protein expressed in the distal nephron epithelium. Claudin-7 has been extensively studied in renal cell carcinoma (RCC) subtypes. By immunohistochemical (IHC) analysis, membranous Claudin-7 expression was detected in 67% of chromophobe RCC, compared with 0% of clear cell RCCs, 28% of papillary RCCs, and 23% oncocytomas. Claudin-7 expression may provide clinical utility in the differential diagnosis of chromophobe RCC and oncocytoma. Hornsby and colleagues examined Claudin-7 IHC and reported 71% and 73% positive and negative predictive values for the differential diagnosis of chromophobe RCC from oncocytoma.

Literature:
1. Hornsby CD, et al. Claudin-7 immunohistochemistry in renal tumors: a candidate marker for chromophobe renal cell carcinoma identified by gene expression profiling.Arch Pathol Lab Med. 2007; 131(10): 1541-6.
2. Lechpammer M, et al. he diagnostic and prognostic utility of claudin expression in renal cell neoplasms. Mod Pathol. 2008; 21(11): 1320-9.
3. Osunkoya AO, et al. Claudin-7 and claudin-8: immunohistochemical markers for the differential diagnosis of chromophobe renal cell carcinoma and renal oncocytoma. Hum Pathol. 2009; 40(2): 206-10.

CXCR4 (Fusin, CD184) (EP394), *rabbit monoclonal*



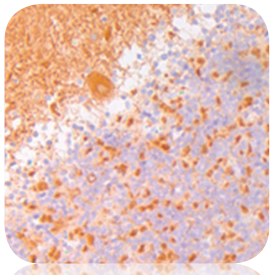
- 0.1 ml concentrate . . . . . #AC-0366RUO
- 1.0 ml concentrate . . . . . #AC-0366RUOC

The chemokine receptor 4 (CXCR4), also known as fusin or stromal cell-derived factor-1 receptor is a member of the C-X-C chemokine receptor family. CXCR4 is activated upon interaction with its endogenous chemokine ligand, CXCL12 (SDF-1). Upon binding, the CXCR4/CXCL12 axis initiate various downstream signaling pathways that increase intracellular calcium, gene transcription, chemotaxis, cell survival and proliferation. CXCR4 is expressed in many types of normal cells. In tumors, CXCR4 is overexpressed in more than 23 different types of human cancers including kidney, lung, brain, prostate, breast, pancreas, ovarian, and melanoma. Experimental evidence demonstrated CXCR4/CXCL12 facilitating cancer cell survival, angiogenesis and enhance tumor migration and metastasis. Elevated CXCR4 expression was identified as a poor prognostic biomarker. Increased CXCR4 expression in breast and prostate carcinomas were associated with an aggressive phenotype and poor survival rates. Levels of CXCR4 were higher in tumor cells compared with adjacent tissues. CXCR4 expression is also associated with therapeutic resistance.

Literature:

1. Caron G, et al. CXCR4 expression functionally discriminates centroblasts versus centrocytes within human germinal center B cells. J Immunol. 2009; 182(12): 7595-602.
2. Chatterjee S, et al. The intricate role of CXCR4 in cancer. Adv Cancer Res. 2014; 124: 31-82.
3. Furusato B, et al. CXCR4 and cancer. Pathol Int. 2010; 60(7): 497-505.
4. Zaitseva MB, et al. CXCR4 and CCR5 on human thymocytes: biological function and role in HIV-1 infection. J Immunol. 1998; 161(6): 3103-13.

GRIA2 (Glutamate Ionotropic Receptor AMPA Type Subunit 2) (EP387), *rabbit monoclonal*



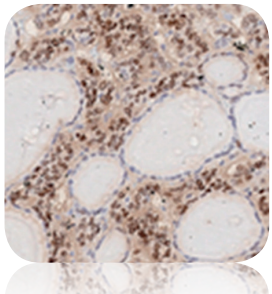
- 0.1 ml concentrate . . . . . #AC-0344A
- 1.0 ml concentrate . . . . . #AC-0344

Glutamate receptor 2 (GRIA2) is a ligand-gated ion channel that uses L-glutamate for excitatory synaptic transmission expressed in the central nervous system. A recent gene expression profiling study reported >100 fold GRIA2 induction in solitary fibrous tumors compared with control tissues. Immunohistochemistry studies demonstrated GRIA2 positivity in the majority of solitary fibrous tumors (64-86%). Its diagnostic performance yields 64% sensitivity, 92% specificity, with 41% and 97% positive and negative predictive value, respectively for the differential diagnosis of solitary fibrous tumors versus other mesenchymal soft tissue tumors. GRIA2 may be a useful marker to identify STAT6-negative solitary fibrous tumors.

Literature:

1. Geramizadeh B, et al. Role of Immunohistochemistry in the Diagnosis of Solitary Fibrous Tumor, a Review. Iran J Pathol. 2016; 11(3): 195-203.
2. Hornick JL, et al. Novel uses of immunohistochemistry in the diagnosis and classification of soft tissue tumors.: Mod Pathol. 2014; 27 Suppl 1: S47-63.
3. Macagno N, et al. Differential Diagnosis of Meningeal SFT-HPC and Meningioma: Which Immunohistochemical Markers Should Be Used? Am J Surg Pathol. 2016; 40(2): 270-8.
4. Ouladan S, et al. Differential diagnosis of solitary fibrous tumors: A study of 454 soft tissue tumors indicating the diagnostic value of nuclear STAT6 relocation and ALDH1 expression combined with in situ proximity ligation assay. Int J Oncol. 2015; 46(6): 2595-605.

HMGA2 (high mobility group AT-hook 2) (EP398), *rabbit monoclonal*



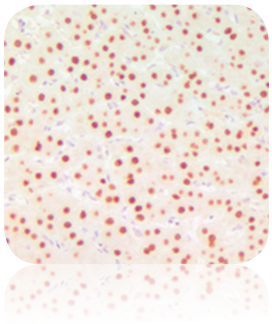
- 0.1 ml concentrate . . . . . #AC-0369A
- 1.0 ml concentrate . . . . . #AC-0369

High-mobility group AT-hook 2 (HMGA2) is a chromatin factor that regulates transcription and cellular differentiation during embryonic development. HMGA2 expression in adult tissues is often associated with benign and malignant tumor formation. HMGA2 is expressed in most conventional and intramuscular lipomas, 84 and 100%, respectively and can aid in differentiating between lipomas from dedifferentiated liposarcomas and distinguishing areas of tumor from normal adipose tissue. In mesenchymal tumors, HMGA2 is expressed in 88% of benign fibrous histiocytoma, 90% of nodular fasciitis, and 90% of vulvovaginal angiomyxoma. The presence of HMGA2 in cancer is correlative with metastasis and poor prognosis.

Literature:

1. Belge G, et al. Upregulation of HMGA2 in thyroid carcinomas: a novel molecular marker to distinguish between benign and malignant follicular neoplasias. Genes Chromosomes Cancer. 2008; 47(1): 56-63.
2. Dreux N, et al. Value and limitation of immunohistochemical expression of HMGA2 in mesenchymal tumors: about a series of 1052 cases. Mod Pathol. 2010; 23(12): 1657-66.
3. Jang MH, et al. The Diagnostic Usefulness of HMGA2, Survivin, CEACAM6, and SFN/14-3-3 δ in Follicular Thyroid Carcinoma. J Pathol Transl Med. 2015; 49(2): 112-7.
4. Motoyama K, et al. Clinical significance of high mobility group A2 in human gastric cancer and its relationship to let-7 microRNA family. Clin Cancer Res. 2008; 14(8): 2334-40.

HNF4 alpha P1 (EP366), *rabbit monoclonal*



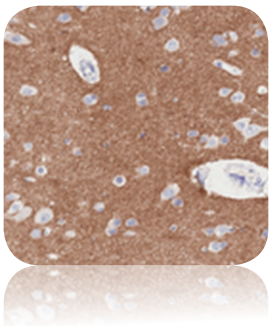
- 0.1 ml concentrate . . . . . #AC-0334A
- 1.0 ml concentrate . . . . . #AC-0334

Hepatocyte nuclear factor-4 alpha (HNF4α) is a member of the nuclear receptor superfamily and is critical for the maintenance of epithelial cell function and normal colon physiology. Isoforms of HNF4α are generated by alternative splicing of the P1 and P2 promoter. HNF4α is critical for the balance between proliferation and differentiation. In normal tissues, HNF4α P1 is localized to the nucleus and expressed in the small intestine, colon, liver, and kidney, but no expression was found in stomach and lung. HNF4α P1 antibody may be useful for subclassification of gastric tumors. In several studies focusing on colorectal carcinoma, HNF4α P1 was shown to be frequently lost in tumor cells. In contrast, HNF4α P2 expression was unaffected.

Literature:

1. Chellappa K, et al. HNF4α: a new biomarker in colon cancer? Biomark Med. 2012; 6(3): 297-300.
2. Takano K, et al. Immunohistochemical staining for P1 and P2 promoter-driven hepatocyte nuclear factor-4alpha may complement mucin phenotype of differentiated-type early gastric carcinoma. Pathol Int. 2009; 59(7): 462-70.
3. Tanaka T, et al. Dysregulated expression of P1 and P2 promoter-driven hepatocyte nuclear factor-4alpha in the pathogenesis of human cancer. J Pathol. 2006; 208(5): 662-72.

L1CAM (Neural Cell Adhesion Molecule L1, CD171) (EP411), *rabbit monoclonal*



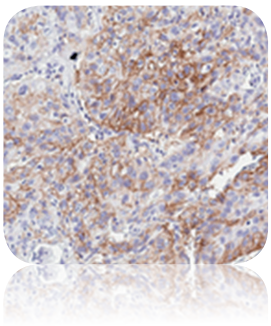
- 0.1 ml concentrate . . . . . #AC-0354RUO
- 1.0 ml concentrate . . . . . #AC-0354RUOC

The L1 Cell Adhesion Molecule (L1CAM), also known as CD171, is a transmembrane glycoprotein crucial for neurogenesis. Mutations in the X-linked L1CAM result in MASA syndrome. In addition to the brain, L1CAM expression is normally expressed in kidney tubular epithelium, intestinal crypt, and peripheral nerves. L1CAM has been investigated in various tumors, including colorectal, renal cell, ovarian, and thyroid carcinomas. Cytoplasmic and membrane expression of L1CAM were significantly correlated with poor clinical outcome, defined with aggressive tumor progression, invasion, and unfavorable prognosis. In a large-scale evaluation of over a thousand early-stage endometrial cancers, 51% of L1CAM-positive tumors experienced recurrence versus 3% of L1CAM-negative tumors. Zeimet and colleagues recommended routine immunohistochemical L1CAM determination for all type I endometrial cancers due to its superiority over classical risk assessment.

Literature:

1. Altevogt P, et al. L1CAM in human cancer. Int J Cancer. 2016; 138(7): 1565-76.
2. Bosse T, et al. L1 cell adhesion molecule is a strong predictor for distant recurrence and overall survival in early stage endometrial cancer: pooled PORTEC trial results. Eur J Cancer. 2014; 50(15): 2602-10.
3. Chen DL, et al. L1cam promotes tumor progression and metastasis and is an independent unfavorable prognostic factor in gastric cancer. J Hematol Oncol. 2013; 6: 43.
4. Kommoss FK, et al. L1CAM further stratifies endometrial carcinoma patients with no specific molecular risk profile. Br J Cancer. 2018 Aug; 119(4): 480-486.
5. Zeimet AG, et al. L1CAM in early-stage type I endometrial cancer: results of a large multicenter evaluation. J Natl Cancer Inst. 2013; 105(15): 1142-50.

LAT1 (L-type amino-acid transporter 1, SLC7AC) (EP393), *rabbit monoclonal*



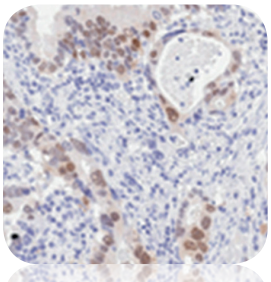
- 0.1 ml concentrate . . . . . #AC-0367RUO
- 1.0 ml concentrate . . . . . #AC-0367RUOC

The L-type amino-acid transporter 1 (LAT1), a heterodimer composed of SLC7A5 and SLC3A2 is a sodium-independent antiporter that functions to uptake neutral amino acids. Clone EP393 is targeted against the SLC7A5 subunit. LAT1 regulates the mTORC1 pathway through leucine transport, making it one of the few amino acid transporters involved in cell growth, survival and proliferation. LAT1 is highly expressed in the brain and retinal endothelium, placenta, testis and skin. It is also detected in the lymph nodes, mammary glands and stomach. Upregulation of LAT1 occurs in a wide spectrum of human cancers, where it is highly expressed in colon, skin, brain, lymph node, and pancreatic cancers. Amplified expression of LAT1 is correlated with high proliferating potential and poor survival. As a prognostic marker, it associates with high-grade cancer staging and malignancy.

Literature:

1. Dickens D, et al. Modulation of LAT1 (SLC7A5) transporter activity and stability by membrane cholesterol. Sci Rep. 2017; 7: 43580.
2. Fuchs BS, et al. Amino acid transporters ASCT2 and LAT1 in cancer: partners in crime? Semin Cancer Biol. 2005; 15(4): 254-66.
3. Kaira K, et al. Prognostic significance of L-type amino acid transporter 1 expression in resectable stage I-III nonsmall cell lung cancer. Br J Cancer. 2008; 98(4): 742-8.
4. Nawashiro H, et al. L-type amino acid transporter 1 as a potential molecular target in human astrocytic tumors. Int J Cancer. 2006; 119(3): 484-92.
5. Yanagida O, et al. Human L-type amino acid transporter 1 (LAT1): characterization of function and expression in tumor cell lines. Biochim Biophys Acta. 2001; 1514(2): 291-302.

MAGEA3 (EP8), *rabbit monoclonal*



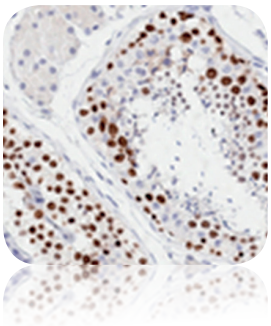
- 0.1 ml concentrate . . . . . #AC-0355RUO
- 1.0 ml concentrate . . . . . #AC-0355RUOC

The melanoma-associated antigen 3 (MAGEA3) is a Cancer/Testis (CT) antigen. MAGEA3 expression is restricted to testicular germ cells in normal adult tissues. It is frequently expressed in over 50% of solid malignancies but is uncommon in leukemia. Due to its unique expression pattern, MAGEA3 is actively investigated as a target for potential immunotherapeutics. MAGEA3 expression was detected in 73% of NSCLC, 58% of urothelial, and 28% of colorectal carcinomas. In NSCLC cases, MAGEA3 expression was not detected in adjacent healthy lung tissue. MAGEA3 expression is significantly associated with lymph node metastasis and advanced (stage III-IV) disease. Overall survival was significantly negatively correlated with MAGEA3 expression.

Literature:

1. Chen X, et al. Expression and prognostic relevance of MAGE-A3 and MAGE-C2 in non-small cell lung cancer. Oncol Lett. 2017; 13(3): 1609-1618.
2. Laban S, et al. MAGE expression in head and neck squamous cell carcinoma primary tumors, lymph node metastases and respective recurrences-implications for immunotherapy. Oncotarget. 2017; 8(9): 14719-14735.
3. Lausenmeyer EM, et al. Strong Expression of Cancertestis Antigens CTAG1B and MAGEA3 Is Correlated with Unfavourable Histopathological Features and MAGEA3 Is Associated with Worse Progression-Free Survival in Urothelial Bladder Cancer. Urol Int. 2018; 1: 1-6.
4. Shantha Kumara HM, et al. MAGE-A3 is highly expressed in a subset of colorectal cancer patients. Cancer Immun. 2012; 12: 16.

MAGEC2 (Melanoma-associated antigen C2, CT10) (EP405), *rabbit monoclonal*



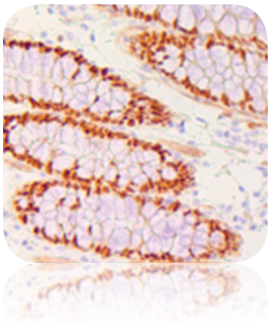
- 0.1 ml concentrate . . . . . #AC-0356A
- 1.0 ml concentrate . . . . . #AC-0356

The Melanoma-associated antigen C2 is a novel Cancer/testis (CT)-antigen which expression is restricted to the testis in normal tissues. Male germ cells highly express MAGEC2 during early phases of spermatogenesis. Bode, et al. examined 325 testicular germ cell tumors and found MAGEC2 in most seminoma (94%), spermatocytic seminoma (100%) and intratubular germ cell neoplasia (IGCNU) (100%). Conversely, MAGEC2 expression were uncommon in embryonal carcinoma, yolk sac tumor, teratoma and choriocarcinoma. MAGEC2 protein expression is a sensitive marker for seminomas, spermatocytic seminomas, and IGCNU. Use of this marker may be helpful in the diagnosing seminoma (positive) from embryonal carcinoma (negative) when assessed in a panel of germ cell tumor markers including OCT4, KIT, PLAP, CD30, SOX2 and SOX17.

Literature:

1. Bode PK, et al. MAGEC2 is a sensitive and novel marker for seminoma: a tissue microarray analysis of 325 testicular germ cell tumors. Mod Pathol. 2011; 24(6): 829-35.
2. Chen X, et al. Expression and prognostic relevance of MAGE-A3 and MAGE-C2 in non-small cell lung cancer. Oncol Lett. 2017; 13(3): 1609-1618.
3. Figueiredo DL, et al. High expression of cancer testis antigens MAGE-A, MAGE-C1/CT7, MAGE-C2/CT10, NY-ESO-1, and gage in advanced squamous cell carcinoma of the larynx.Head Neck. 2011; 33(5): 702-7.
4. von Boehmer L, et al. Frequent expression of the novel cancer testis antigen MAGE-C2/CT-10 in hepatocellular carcinoma.PLoS One. 2011; 6(7): e21366.
5. Zhao Q, et al. Pilot Study on MAGE-C2 as a Potential Biomarker for Triple-Negative Breast Cancer. Dis Markers. 2016; 2016: 2325987.

MCM6 (EP375), *rabbit monoclonal*



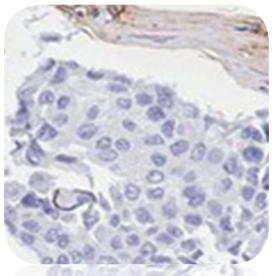
- 0.1 ml concentrate . . . . . #AC-0340RUO
- 1.0 ml concentrate . . . . . #AC-0340RUOC

Six main highly conserved DNA-binding members (MCM2 to -7) have been well documented to interact with each other, forming a heterohexamer complex. Upon activation by cyclin-dependent kinases, MCM proteins bind to chromatin in late mitosis and G1 and lead to initiation of DNA synthesis. MCM proteins disassociate from chromatin after DNA replication to restrict chromosome replication to one round per cell cycle. MCM proteins have been suggested as potentially important biomarkers for cancer diagnosis and prognosis. High MCM6 expression was associated with a significantly shorter survival in mantle cell lymphoma. Increased MCM6 labeling was also associated with chondrosarcoma histopathological grade. Further, it was shown to be more effective in identifying proliferative activity compared to Ki-67. Examination of a combination of MCM2 to -7 demonstrated significantly diminished survival when four or more MCM are overexpressed in ER+ breast cancers.

Literature:

1. Liu M, et al. MCM6 promotes metastasis of hepatocellular carcinoma via MEK/ERK pathway and serves as a novel serum biomarker for early recurrence. J Exp Clin Cancer Res. 2018; 37(1): 10.
2. Hotton J, et al. Minichromosome maintenance complex component 6 (MCM6) expression correlates with histological grade and survival in endometrioid endometrial adenocarcinoma. Virchows Arch. 2018; 472(4): 623-633.
4. Kwok HF, et al. Prognostic significance of minichromosome maintenance proteins in breast cancer. Am J Cancer Res. 2014 5(1): 52-71.
5. Vigouroux C, et al. Methyl(R217)HuR and MCM6 are inversely correlated and are prognostic markers in non small cell lung carcinoma. Lung Cancer. 2015, 89(2): 189-96.

MFAP5 (Microfibrillar-associated protein 5) (EP382), *rabbit monoclonal*



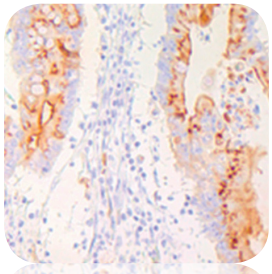
- 0.1 ml concentrate . . . . . #AC-0348RUO
- 1.0 ml concentrate . . . . . #AC-0348RUOC

The microfibrillar-associated protein 5 (MFAP5), alternatively known as microfibril-associated glycoprotein 2 (MAGP2) is a glycoprotein involved in microfibril assembly and modulates endothelial cell motility. Recently, MFAP5 was considered as a novel modulator in cell survival. Elevated MFAP5 expression was reported in head, neck, pancreatic, lung and ovarian cancers. In ovarian cancer, MFAP5 was determined as an independent predictor of tumor survival and proliferation. High MFAP5 mRNA and protein levels stratified the low and high risk patient groups, with positive MFAP5 predicting a poor prognosis. Elevated MFAP5 levels also correlate with chemo-resistance and predict poor prognosis.

Literature:

1. Leung CS, et al. Calcium-dependent FAK/CREB/TNNC1 signalling mediates the effect of stromal MFAP5 on ovarian cancer metastatic potential.Nat Commun. 2014; 5: 5092.
2. Spivey KA, et al. A prognostic gene signature in advanced ovarian cancer reveals a microfibril-associated protein (MAGP2) as a promoter of tumor cell survival and angiogenesis Cell Adh Migr. 2010; 4(2): 169-71.
3. Yang X, et al. MFAP5 and TNNC1: Potential markers for predicting occult cervical lymphatic metastasis and prognosis in early stage tongue cancer: Oncotarget. 2017; 8(2): 2525-2535.
4. WU Z, et al. MFAP5 promotes tumor progression and bone metastasis by regulating ERK/MMP signaling pathways in breast cancer. Biochem Biophys Res Commun. 2018; 498(3): 495-501.

MMP-7 (Matrix-Metalloproteinase-7, Matrilysin) (EP388), *rabbit monoclonal*



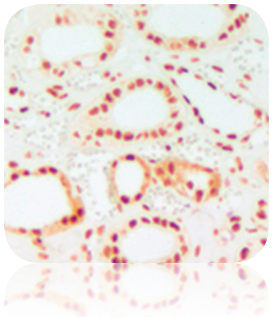
- 0.1 ml concentrate . . . . . #AC-0346RUO
- 1.0 ml concentrate . . . . . #AC-0346RUOC

The matrix metalloproteinase-7 (MMP-7), is a member of the MMP family of zinc- and calcium-dependent endopeptidases that degrade matrix glycoproteins. MMP-7 may play an important role in tumor invasion and metastases. It is produced in neoplastic cells and upregulated during neoplastic growth. MMP-7 expression was reported to be produced by malignant tumor cells in esophageal, gastric, colorectal, head and neck, lung, prostate and hepatocellular carcinoma. Immunohistochemical studies have shown MMP-7 expression association with the depth of tumor invasion, advanced tumor stage, and recurrence. Progressive MMP-7 expression was observed in the transition from normal to adenomatous to carcinomatous colonic mucosa, and overexpressed in 85% of colorectal adenocarcinomas. Overexpression of MMP-7 is typically associated with poor prognosis.

Literature:

1. Masaki T, et al. Matrilysin (MMP-7) as a significant determinant of malignant potential of early invasive colorectal carcinomas. Br J Cancer. 2001; 84(10): 1317-21.
2. Qasim BJ, et al. Immunohistochemical expression of matrix metalloproteinase-7 in human colorectal adenomas using specified automated cellular image analysis system: A clinicopathological study Saudi J Gastroenterol. 2013; 19(1): 23-7.
3. Omar AH, et al. MMP-7, MMP-8, and MMP-9 in oral and cutaneous squamous cell carcinomas. Oral Surg Oral Med Oral Pathol Oral Radiol. 2015; 119(4): 459-67.

PBRM1 (BAF180) (EP342), *rabbit monoclonal*



- 0.1 ml concentrate . . . . . #AC-0333RUO
- 1.0 ml concentrate . . . . . #AC-0333RUOC

PBRM1 encodes protein polybromo-1 (also referred to as BAF180), a subunit of the SWI/SNF transcription-modulating chromatin remodeling complex. This complex is responsible in the mobilization of nucleosomes by modulating movement of histones from chromatin. PBRM1 and BAP1 are the two most commonly mutated genes in clear cell renal cell carcinoma (ccRCC). Truncating mutations in PBRM1 are found in 41% of ccRCC and loss of PBRM1 protein expression is associated with tumor progression. In one study, PBRM1 deficient tumors were associated with worse tumor size, grade, invasion and higher risk of metastasis. Negative PBRM1 tumors have significantly decreased disease-free and recurrence-free survival rates, demonstrating its utility as a marker of poor prognosis.

Literature:

1. Högner A, et al. PBRM1 and VHL expression correlate in human clear cell renal cell carcinoma with differential association with patient's overall survival. Urol Oncol. 2018; 36(3): 94.e1-94.e14.
2. Brugarolas J. PBRM1 and BAP1 as novel targets for renal cell carcinoma. Cancer J. 2013; 19(4): 324-32.
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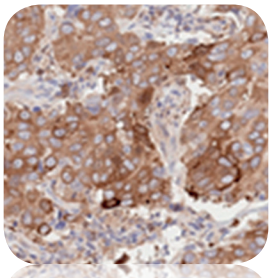
4. Kapur P, et al. Effects on survival of BAP1 and PBRM1 mutations in sporadic clear-cell renal-cell carcinoma: a retrospective analysis with independent validation. Lancet Oncol. 2013; 14(2): 159-67.

Sequestosome-1 (SQSTM1 gene, ubiquitin-binding protein p62) (EP396), *rabbit monoclonal*



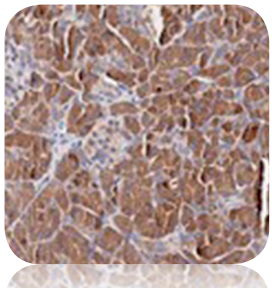
- 0.1 ml concentrate . . . . . #AC-0368A
- 1.0 ml concentrate . . . . . #AC-0368

Sequestosome-1, is an ubiquitin-binding adapter protein involved during autophagy which is typically degraded during the autophagy process. Presence of Sequestosome-1 cytosolic aggregate is used as a marker for autophagy deficiency. Sequestosome-1 immunohistochemistry (IHC) is useful for identifying hepatocellular carcinoma (HCC) as it demonstrates superior sensitivity for HCC compared against glypican-3. Positive Sequestosome-1 staining was found in 100% of HCC but was negative in all non-tumor areas and cirrhotic nodules. Furthermore, a panel consisting of Sequestosome-1, aminoacylase 1, and glypican-3 provides high sensitivity (93.8%) and specificity (95.2%) in the differential diagnosis between well differentiated HCC and high grade dysplastic nodules. Sequestosome-1 expression can also aid in diagnosing drug-induced autophagic vacuolar myopathies.

Literature:

1. Jin GZ, et al. A novel panel of biomarkers in distinction of small well-differentiated HCC from dysplastic nodules and outcome values. BMC Cancer. 2013; 13: 161.
2. Schläfli AM, et al. Prognostic value of the autophagy markers LC3 and p62/SQSTM1 in early-stage non-small cell lung cancer. Oncotarget. 2016; 7(26): 39544-39555.
3. Burdelski C, et al. Cytoplasmic Accumulation of Sequestosome 1 (p62) Is a Predictor of Biochemical Recurrence, Rapid Tumor Cell Proliferation, and Genomic Instability in Prostate Cancer. Clin Cancer Res. 2015; 21(15): 3471-9.
4. Lee HS, et al. Clinical Utility of LC3 and p62 Immunohistochemistry in Diagnosis of Drug-Induced Autophagic Vacuolar Myopathies: A Case-Control Study. PLoS One. 2012; 7(4): e36221.

SPINK1 (TATI, PSTI) (EP401), *rabbit monoclonal*



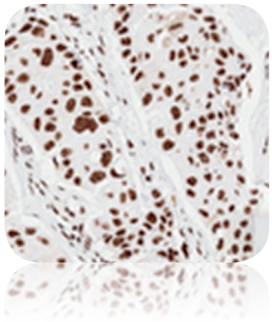
- 0.1 ml concentrate . . . . . #AC-0363A
- 1.0 ml concentrate . . . . . #AC-0363

Serine protease inhibitor Kazal-type 1 (SPINK1), also known as tumor-associated trypsin inhibitor (TATI) and pancreatic secretory trypsin inhibitor (PSTI) is a cytosolic trypsin inhibitor secreted by pancreatic acinar cells and foveolar cells of the stomach that protects the gastrointestinal system from premature trypsinogen auto-digestion. Mutations in SPINK1 are associated with hereditary pancreatitis. Recently, SPINK1 demonstrated utility in differentiating hepatocellular carcinoma (HCC) from precancerous lesions. SPINK1 expression is also detected in neoplasms of the ovary, bladder, kidney, pancreas, colon, lung, and breast. High expression of SPINK1 is often associated with advanced tumor staging, making it a useful prognostic marker.

Literature:

1. Brooks JD, et al. Evaluation of ERG and SPINK1 by Immunohistochemical Staining and Clinicopathological Outcomes in a Multi-Institutional Radical Prostatectomy Cohort of 1067 Patients. PLoS One. 2015; 10(7): e0132343.
2. Flavin R, et al. SPINK1 protein expression and prostate cancer progression. Clin Cancer Res. 2014; 20(18): 4904-11.
3. Marshall A, et al. Global Gene Expression Profiling Reveals SPINK1 as a Potential Hepatocellular Carcinoma Marker PLoS One. 2013; 8(3): e59459.
4. Rink M, et al. Loss of SPINK1 expression is associated with unfavorable outcomes in urothelial carcinoma of the bladder after radical cystectomy. Urol Oncol. 2013; 31(8): 1716-24.

Splicing Factor 3B subunit 3 (SF3B3) (EP404), *rabbit monoclonal*



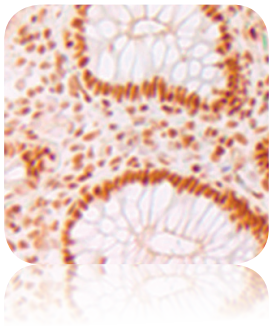
- 0.1 ml concentrate . . . . . #AC-0358RUO
- 1.0 ml concentrate . . . . . #AC-0358RUOC

The splicing factor 3B subunit 3 (SF3B3) is an integral part of the splicing factor 3b and together with splicing factor 3a a key component of the core splicesome complex. The splicesome is responsible for binding pre-mRNA and excision of introns to form mature mRNA. A growing body of evidence suggests that splicing factors may provide prognostic utility in cancers, including breast and hepatocellular carcinomas. Gökmen-Polar, et al. recently demonstrated significantly higher SF3B3 expression in ER-negative tumors compared with ER-positive. In the ER-positive subset, upregulation of SF3B3 was associated with higher-recurrence scores, poor relapse-free survival and shorter overall survival. Clone EP404 is targeted against residues near the C-terminus of SF3B3.

Literature:

1. Ke Chen, et al. Alternative splicing of EZH2 pre-mRNA by SF3B3 contributes to the tumorigenic potential of renal cancer. Clin Cancer Res. 2017; 23(13): 3428-3441.
2. Choi JH, et al. Mutations acquired by hepatocellular carcinoma recurrence give rise to an aggressive phenotype. Oncotarget. 2017; 8(14): 22903-22916.
3. Gökmen-Polar Y, et al. Expression levels of SF3B3 correlate with prognosis and endocrine resistance in estrogen receptor-positive breast cancer. Mod Pathol. 2015; 28(5): 677-85.

STAG2 (Cohesin subunit SA2) (EP373), *rabbit monoclonal*



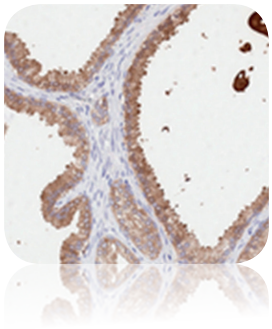
- 0.1 ml concentrate . . . . . #AC-0339RUO
- 1.0 ml concentrate . . . . . #AC-0339RUOC

Cohesin subunit SA2, encoded by the gene STAG2 yields a 141-kDa subunit of cohesin. The primary function of the cohesin multimeric complex is to mediate genome-wide sister chromatid cohesion after DNA replication to ensure proper segregation during mitosis. STAG2 was reported to be a commonly mutated tumor suppressor gene in glioblastoma, urothelial carcinoma, acute myeloid leukemia and Ewing family tumors. Almost all tumor-derived STAG2 mutations discovered are truncating mutations and its high frequency of mutation may be reflective of its location on the X chromosome, requiring only a single mutation for its inactivation. Prognostic significance of cohesin SA2 status in tumors is still under debate. STAG2 loss was associated with increased disease-free survival in non-muscle invasive urothelial carcinoma. Conversely, its loss was significantly associated with an increase of disease recurrence and mortality in invasive urothelial carcinomas.

Literature:

1. Balbás-Martínez C, et al. Recurrent inactivation of STAG2 in bladder cancer is not associated with aneuploidy. Nat Genet. 2013; 45(12): 1464-9.
2. Brohl AS, et al. The genomic landscape of the Ewing Sarcoma family of tumors reveals recurrent STAG2 mutation. PLoS Genet. 2014; 10(7): e1004475.
3. Mehta GD, et al. Cohesin: functions beyond sister chromatid cohesion. FEBS Lett. 2013; 587(15): 2299-312.
4. Solomon DA, et al. Mutational inactivation of STAG2 causes aneuploidy in human cancer. Science. 2011; 333(6045): 1039-43.
5. Solomon DA, et al. Frequent truncating mutations of STAG2 in bladder cancer. Nat Genet. 2013; 45(12): 1428-30.

TIMP-1 (EP389), *rabbit monoclonal*



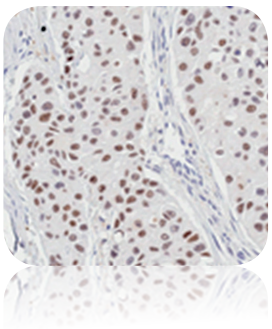
- 0.1 ml concentrate . . . . . #AC-0359RUO
- 1.0 ml concentrate . . . . . #AC-0359RUOC

The tissue inhibitor of metalloproteinase 1 (TIMP-1) is a 28 kDa glycoprotein that binds and inhibits matrix metalloproteinases (MMPs). An imbalance of MMPs and TIMPs has been shown to play an important role in tumor invasion and metastasis. TIMP-1 expression is detected in the cytoplasm in tumor cells. High TIMP-1 within tumors is associated with reduced disease-free and overall survival in non-Hodgkin's lymphoma, colorectal, prostate, urothelial, lung and breast cancers. Heterogeneous TIMP-1 protein expression was detected in non-small cell lung carcinomas, and overexpression was associated with high p53 expression and adverse clinical outcomes. Similarly, elevated levels of MMP-9 and TIMP-1 were significantly associated with lymph node metastasis and advanced tumor stage in breast cancer.

Literature:

1. Aaberg-Jessen C, et al. Comparative studies of TIMP-1 immunohistochemistry, TIMP-1 FISH analysis and plasma TIMP-1 in glioblastoma patients. J Neurooncol. 2016; 130(3): 439-448.
2. Aljada IS, et al. Upregulation of the tissue inhibitor of metalloproteinase-1 protein is associated with progression of human non-small-cell lung cancer. J Clin Oncol. 2004; 22(16): 3218-29.
3. Holten-Andersen MN, et al. Total levels of tissue inhibitor of metalloproteinases 1 in plasma yield high diagnostic sensitivity and specificity in patients with colon cancer. Clin Cancer Res. 2002; 8(1): 156-64.
4. Holten-Andersen MN, et al. Localization of tissue inhibitor of metalloproteinases 1 (TIMP-1) in human colorectal adenoma and adenocarcinoma. Int J Cancer. 2005; 113(2): 198-206.

TRPS1 (EP392), *rabbit monoclonal*



- 0.1 ml concentrate . . . . . #AC-0360RUO
- 1.0 ml concentrate . . . . . #AC-0360RUOC

TRPS1 is an atypical member of the GATA family of transcription factor, which represses transcription of GATA sequence containing genes. Studies have implicated TRPS1 in several malignant tumors, including osteosarcoma, breast and colon cancers. TRPS1 upregulation was significantly associated with higher pathological stage and positive lymph node and distant metastasis. Survival analysis correlated high TRPS1 expression with both shorter overall and disease-free survival rates. TRPS1 is associated with tumor growth, invasion and metastasis. Overexpression of TRPS1 correlated with higher microvessel density (MVD) in breast cancer, as detected by CD31 staining. These results support the role of TRPS1 in pathological angiogenesis and promotion of aggressive phenotypes.

Literature:

1. Li Z, et al. Overexpression of Trps1 contributes to tumor angiogenesis and poor prognosis of human osteosarcoma. Diagn Pathol. 2015; 10: 167.
2. Lin HY, et al. GATA3 and TRPS1 are distinct biomarkers and prognostic factors in breast cancer: database mining for GATA family members in malignancies. Oncotarget. 2017; 8(21): 34750-34761.

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Notes

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