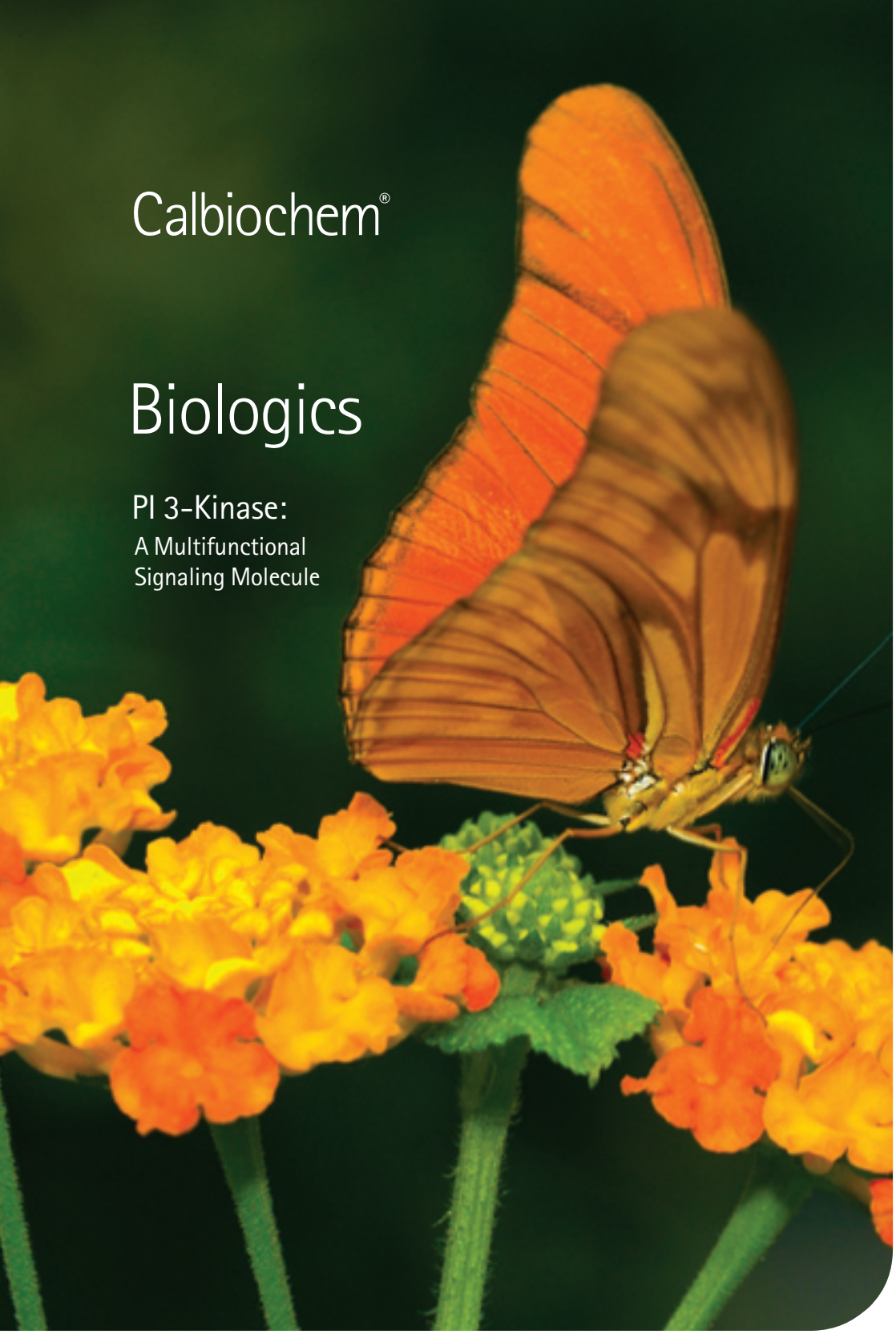


Calbiochem®

Biologics

PI 3-Kinase:
A Multifunctional Signaling Molecule

Volume 33, No. 2, 2007

Inside this issue...

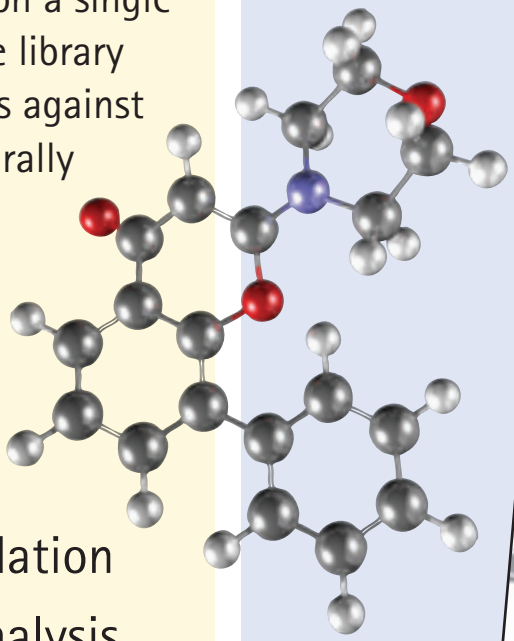
EMD

Calbiochem®

Protein Kinase Inhibitor Library

Cat. No. 539744

The **InhibitorSelect™ Protein Kinase Inhibitor Library** includes 80 well-characterized protein kinase inhibitors on a single 96-well plate. The library includes inhibitors against a panel of structurally diverse protein kinases.



Suitable for:

- ✔ Target validation
- ✔ Pathway analysis
- ✔ Assay development
- ✔ Kinase screening

Targets: Akt; AMPK; Aurora; DNA-PK; IRAK; PKC; Rho; TGF-βR; Bcr-Abl; EGFR; FLT3; FMS; IGFR; JAK; Lck; Met; PDGFR; Src; Syk; VEGFR; and PI 3-K

Visit our website for more information:

www.calbiochem.com/inhibitorkinaselibrary

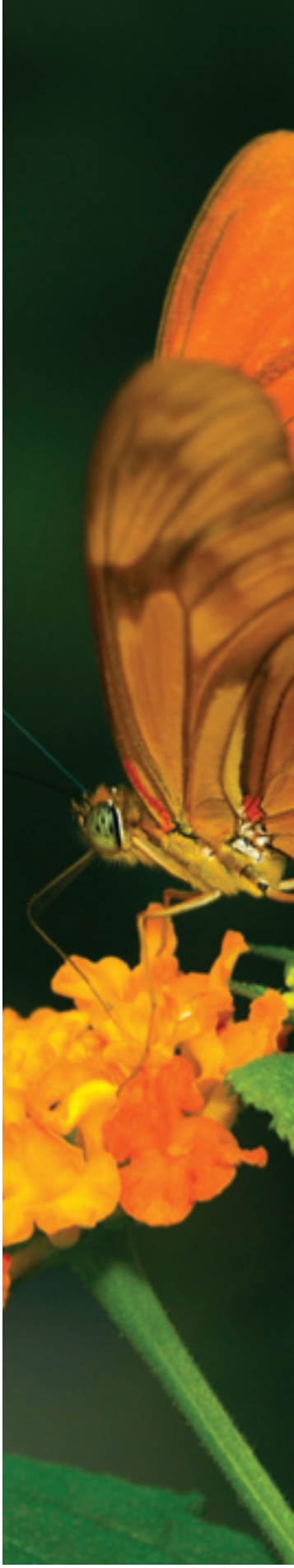
Plate Features	Inhibitor Features	Documentation
96-well format	Convenient, ready-to-use	Structure SD-files
10 mM DMSO solution	Cell-permeable	Published IC_{50} values
50 µl/well	Majority are ATP-competitive	CAS numbers
Polypropylene plate	Stable in DMSO	Literature citations
Tight robolid silicone seal	Structurally most diverse selection	PubChem ID
Non-pyrogenic	Multiple inhibitors against selected targets	Inhibitor description

All inhibitor solutions have ≥95% purity (HPLC). Lot specific data for every inhibitor in solution is available.

Phosphoinsositide 3-Kinase (PI 3-K):

A Multifunctional Signaling Molecule

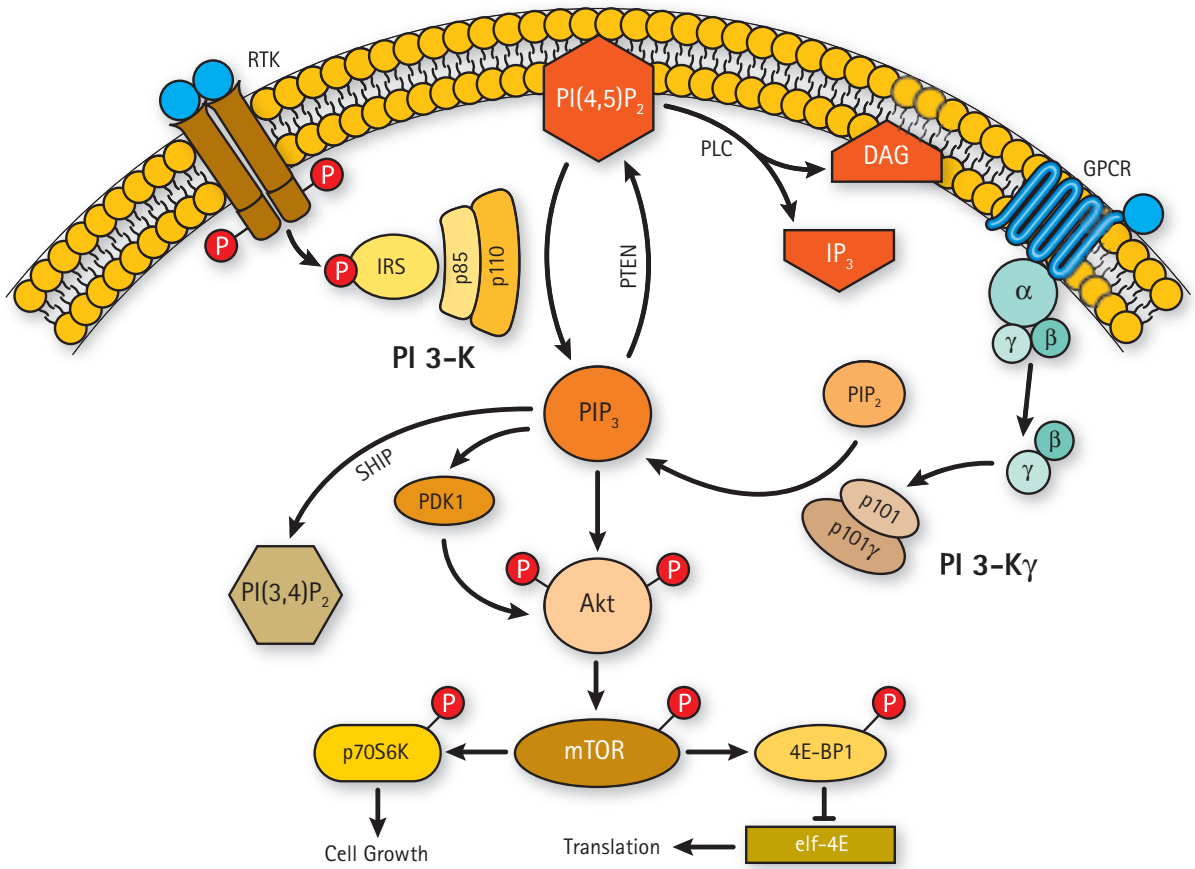
Chandra Mohan, Ph.D., EMD Chemicals, San Diego, California 92121



The PI 3-kinases are ubiquitous enzymes that play a crucial role in the regulation of many cellular processes, including cell growth, proliferation, motility, and survival. The PI 3-kinase family constitutes a large family of lipid and serine/threonine kinases, which includes a number of phosphatidylinositol kinases, as well as the ATM and ATR kinases. PI 3-kinases are divided into three classes based on their structure and substrate specificity. Class I PI 3-kinases, the best studied class, were the first to be characterized and include receptor-regulated heterodimeric enzymes, which contain a 110 kDa catalytic subunit and an 85 kDa regulatory subunit. The class IA PI 3-kinases (p110α, p110β and p110δ isozymes) associate with an 85 kDa adapter/regulatory subunit that is essential for interaction of these PI 3-kinases with receptor tyrosine kinases and intracellular proteins, such as PKC, SHP1, Rac, and Rho. The class IB PI 3-kinases (p110γ) are activated by heterotrimeric G protein βγ-subunits and associate with a p101 adapter/regulatory subunit that is important for full responsiveness to $G_{\beta\gamma}$ heterodimers. PI 3-kinases of both class IA and IB are also activated by Ras. They can use PI, PI (4)P and PI (4,5)P_2 as substrates *in vitro*. Their major *in vivo* substrate appears to be PI(4,5)P_2. The members of this class are sensitive to wortmannin. Class II PI 3- kinases are larger monomeric enzymes (~170 kDa) and show variable responses to wortmannin. They lack the adapter/regulatory subunit and use PI and PI(4)P as substrates. This class of enzymes contains a C-2 domain at the C-terminal region that binds phospholipids in a Ca^{2+}-dependent manner. They are known to participate in integrin signaling in platelets. Three isoforms of class II PI 3-kinases have been described in mammals: the ubiquitously expressed PI 3-kinase C2α and PI 3-kinase C2β, and a liver-specific PI 3-kinase C2γ. PI 3-kinases of class III are heterodimeric enzymes consisting of an adaptor unit, p150 and catalytic subunit Vps34 of 100 kDa size, which can phosphorylate PI(3)P. The human homolog of Vps34 is reported to be sensitive to wortmannin and participates in the regulation of endocytic membrane trafficking and in the regulation of autophagy.

Following ligand binding to receptor and activation of receptor tyrosine kinase, the p85/p110 complex is recruited to the receptor by interaction of the SH2 domain of p85 with consensus phosphotyrosine residues on receptor tyrosine kinase. This allows the p110 catalytic subunit to come in close proximity to its lipid substrates in the cell membrane. The interaction of a receptor tyrosine kinase with the p85 subunit relieves the inhibitory effect of p85 on the p110 catalytic subunit. Activated PI 3-kinase phosphorylates phosphoinositol (PI) substrates to produce PI(3)P, PI(3,4)P2, and PI(3,4,5)P3 (PIP_3). These molecules act as second messengers and recruit the PI 3-kinase-dependent serine/threonine kinases (PDK1) and Akt from the cytoplasm to the plasma membrane. Lipid binding and membrane translocation of Akt leads to conformational changes, which allow it to become phosphorylated on Thr^{308} in the activation loop and Ser^{473} in the hydrophobic phosphorylation motif by PDK1 and PDK2. This dual phosphorylation causes full activation of Akt. ▶▶

Technical Support
Phone 800 628 8470
E-mail calbiochem@emdchemicals.com



The PI 3-kinase pathway diverges at many points in the metabolic scheme, resulting in a variety of physiological effects. PI 3-kinase activation of Akt and subsequent activation of mTOR stimulates cell proliferation and the translation process in response to nutrients and growth factors. It phosphorylates p70S6 kinase and 4E-binding protein (4E-BP). Phosphorylation of 4E-BP allows the release of translation initiation factor, elF4E. The PI 3-kinase/Akt pathway is also involved in the LKB1-mediated activation of AMP-activated protein kinase (AMPK) that inhibits mTOR activity, thereby allowing energy conservation in the cell. Akt also phosphorylates $p21^{WAF1}$ and $p27^{KIP1}$, allowing them to be exported to the cytoplasm for sequestration and degradation. This allows cell proliferation to proceed unimpeded. Several other proteins have also been identified as intracellular targets of PI 3-kinase/Akt.

Class IA PI 3-kinase signaling is considered to be important in mediating insulin responses in cells. Any loss in the activity of these kinases can result in metabolic defects linked to type 2 diabetes. Inhibition of PI 3-kinase and overexpression of dominant negative PI 3-kinase mutants are shown to block many of the physiological responses to insulin. Pharmacological inhibition of PI 3-kinase by wortmannin or LY294002 is shown to diminish insulin-stimulated translocation of GLUT4 to the cell surface and reduce glucose uptake into cells. Overexpression of constitutively active forms of PI 3-kinase p110 catalytic subunit stimulates insulin-mediated metabolic effects and dominant-negative p85 regulatory subunit constructs block insulin-mediated metabolic effects. Akt2, a downstream target of PI 3-kinase, is highly expressed in insulin-responsive tissues, such as muscle and adipose tissue, and is essential for the maintenance of glucose homeostasis. Mice deficient in Akt2 display classical features of type 2 diabetes.

Under resting conditions, PIP_3 levels are practically undetectable in mammalian cells. Levels of PIP_3 are controlled tightly by the action of several PIP_3 phosphatases, such as PTEN, SHIP1, and SHIP2. PTEN acts on the 3-position to convert PIP_3 back to $PI(4,5)P_2$ (PIP_2). On the other hand, the SHIP phosphatases remove phosphate from the 5-position to produce $PI(3,4)P_2$. PIP_2 can also function as a second messenger to recruit PH-domain-containing proteins, such as Akt. Overexpression of PTEN is sufficient to lower basal levels of 3'-phosphorylated phosphoinositide in cells. $PTEN^{-/-}$ mice exhibit higher levels of 3'-phosphorylated phospholipids and die during embryogenesis due to the

Phosphoinsositide 3-Kinase (PI 3-K) *(continued...)*

failure of developmental apoptosis. PTEN$^{-/-}$ mouse embryo fibroblasts are shown to be resistant to apoptotic stimuli. Deletion of SHIP also leads to an increase in PIP_3 levels and a decrease in PIP_2 levels. SHIP$^{-/-}$ mice are also shown to have defective apoptotic machinery and excessive cell survival in the myeloid lineages.

PI 3-kinase signaling is crucial to many aspects of cell growth and survival and this pathway is stimulated by many growth factors. Hence, PI 3-kinase activity is tightly regulated in normal cells. Overactivation of this pathway can perturb the control mechanisms for cell growth and survival and contribute to metastatic competence and resistance to chemotherapy. Abnormal activation of PI 3-kinases is seen in several forms of cancer. About 30% of solid tumors contain mutations in the catalytic unit of their PI 3-kinase, which increases its enzymatic activity and produces excessive Akt signaling. Somatic missense mutations in the p110α gene are reported in HER2-amplified and hormone-receptor-positive breast cancers. Also, p110α is frequently overexpressed and mutated in gliomas, colon, prostate, and gynecological tumors. Several tumors also exhibit either defective or diminished activity in the tumor suppressor, PTEN. Deletion of PTEN in T cells or B cells is shown to enhance their proliferation. Mice heterozygous for PTEN show a predisposition for developing leukemia and lymphoma. Additionally, PI 3-kinase inhibitors, wortmannin and LY294002 exhibit antitumor activities and sensitize tumor cells to chemotherapeutic agents. Given the importance of the PI 3-kinase signaling pathway, several new drug candidates are being sought. A few isoform-selective inhibitors have also been identified. Stable, water-soluble conjugates of wortmannin are being developed to improve its pharmacological characteristics. ■

References:

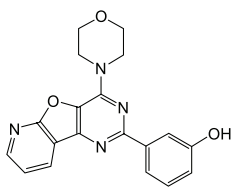
Ito, K., et al. 2007. *J. Pharmacol. Exp. Therap.* **321,** 1.
Medina-Tato, D.A., et al. 2007. *Immunology* **121,** 448.
Leslie, N.R. 2006. *Antioxid. Redox Signal.* **8,** 1765.
Workman, P., et al. 2006. *Nat. Biotech.* **24,** 794.
Samuels, Y., and Ericson, K. 2006. *Curr. Opin. Oncol.* **18,** 77.
Bader, A.G., et al. 2005. *Nat. Rev. Cancer* **5,** 921.
Hennessy, B.T., et al. 2005. *Nat. Drug Disc.* **4,** 988.
Fruman, D.A. 2004. *Biochem. Soc. Trans.* **32,** 315.
Scheid, M.P., and Woodgett, J.R. 2003. *FEBS Lett.* **546,** 108.
Lawlor, M.A., and Alessi, D.R. 2001. *J. Cell Sci.* **114,** 2903.
Toker, A., and Newton, A.C. 2000. *J. Biol. Chem.* **275,** 8271.
Stein, R.C, and Waterfield, M.D. 2000. *Mol. Med. Today* **6,** 347.
Datta, S.R., et al. 1999. *Genes Dev.* **13,** 2905.
Dong, Z., et al. 1999. *Anticancer Res.* **19,** 3743.
Prior, I.A., and Clague, M.J. 1999. *Mol. Cell Biol. Res. Commun.* **1,** 162.
Shepherd, P.R., et al. 1996. *J. Mol. Endocrinol.* **17,** 175.

NEW Inhibitors for PI 3-Kinase/Akt Signaling Pathway

PI-103

(3-(4-(4-Morpholinyl)pyrido[3',2':4,5]furo[3,2-d]pyrimidin-2-yl)phenol)

A cell-permeable potent and ATP-competitive inhibitor of DNA-PK, PI 3-K, and mTOR (IC_{50} = 2, 8, 88, 48, 150, 26, 20, and 83 nM for DNA-PK, p110α, p110β, p110δ, p110γ, PI 3-KC2β, mTORC1, and mTORC2, respectively). *Purity: ≥97% by HPLC.* M.W. 348.4



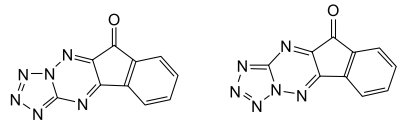
Cat. No.		
528100	1 mg	$99
	5 mg	$364

Ref.: Raynaud, F.I., et al. 2007. *Cancer Res.* **67,** 5840; Fan, Q.W., et al. 2006. *Cancer Cell* **9,** 341; Knight, Z.A., et al. 2006. *Cell* **125,** 733.

PDK1/Akt/Flt Dual Pathway Inhibitor

(6H-Indeno[1,2-e]tetrazolo[1,5-b][1,2,4]triazin-6-one & 10H-Indeno[2,1-e]tetrazolo[1,5-b][1,2,4]triazin-10-one)

A cell-permeable, direct inhibitor of both PDK1 and Akt that blocks phosphorylation of Akt at both Ser^{473} and Thr^{308}. The dual inhibition nature against both PDK1/Akt and Flt3/PIM signaling pathways allows effective killing of AML cells (Average IC_{50} = 1.05, 1.91, and 0.43 µM for AML with wild-type Flt3, single mutant ITD/D835, and double mutant Flt3-ITD-TDK, respectively) that are otherwise resistant to inhibitors targeting only the PDK1/Akt pathway. *Purity: ≥98% by HPLC (sum of two isomers).* M.W. 224.2



Cat. No.		
521275	5 mg	$234

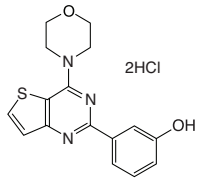
Ref.: Zeng, Z., et al. 2006. *Cancer Res.* **66,** 3737; Koul, D., et al. 2006. *Mol. Cancer Ther.* **5,** 637; Mandal. M., et al. 2006. *Oral Oncol.* **42,** 430; Mandal. M., et al. 2005. *Br. J. Cancer* **92,** 1899.

NEW Inhibitors for PI 3-Kinase/Akt Signaling Pathway *(continued...)*

PI 3-Kα Inhibitor IV

(3-(4-Morpholinothieno[3,2-d]pyrimidin-2-yl)phenol, HCl)

A cell-permeable, potent, and isoform-selective inhibitor of PI 3-kinases (IC_{50} = 2 nM, 16 nM, 660 nM, and 220 nM for p110α, p110β p110γ, and PI 3-K C2β, respectively) and inhibits non-PI 3-K kinases only at much higher concentrations (IC_{50} ≥3.4 µM for Cdk2/E, KDR, PKA, and PKCα). *Purity: ≥95% by HPLC.* M.W. 386.3



Cat. No. 528111 **5 mg** **$185**

Ref.: Hayakawa, M., et al. 2006. *Bioorg. Med. Chem.* **14,** 6847.

PI 3-Kα Inhibitor VIII

(1E-Bromoimidazopyridinyl-methylene-methyl-methyl-nitrobenzenesulfonohydrazide, HCl)

A cell-permeable, potent PI 3-Kα selective inhibitor (IC_{50} = 0.3 nM, 40 nM, 100 nM and 850 nM for p110α, p110γ, PI 3-K C2β, and p110β, respectively). *Purity: ≥95% by HPLC.* M.W. 524.8

Cat. No. 528116 **5 mg** **$185**

Ref.: Hayakawa, M., et al. 2006. *Bioorg. Med. Chem.* **15,** 5837.

PI 3-Kγ Inhibitor VII

(5-(Benzo[1,3]dioxol-5-ylmethylene)-thiazolidine-2,4-dione)

A cell-permeable, potent, and ATP-competitive inhibitor of PI 3-Kγ (IC_{50} = 70 nM) with moderate selectivity over PI 3-Kα, β, and δ isoforms (IC_{50} = 0.24 µM, 1.45 µM and 1.70 µM, respectively). *Purity: ≥98% by HPLC.* M.W. 249.2

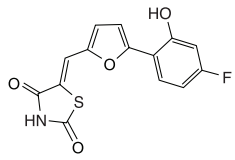
Cat. No. 528114 **5 mg** **$130**

Ref.: Ferrandi, C., et al. 2007. *J. Pharmacol. Exp. Ther.* **322,** 923.

PI 3-Kγ/CKII Inhibitor

(5-(4-Fluoro-2-hydroxyphenyl)furan-2-ylmethylene)thiazolidine-2,4-dione

A cell-permeable, potent, and ATP-competitive inhibitor of PI 3-Kγ and CKII (IC_{50} = 20 nM). It inhibits other PI 3-K isotypes (IC_{50} = 0.94, 20, and 20 µM for α, β, δ, respectively) and MKK7β (IC_{50} >10 µM) only at much higher concentrations. *Purity: ≥98% by HPLC.* M.W. 305.3

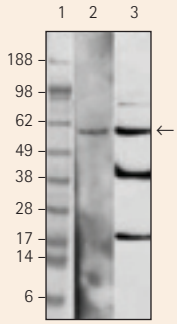


Cat. No. 528112 **5 mg** **$140**

Ref.: Pomel, V., et al. 2006. *J. Med. Chem.* **49,** 3857.

Anti-PDK1 (1-556) Rabbit pAb

Polyclonal IgG, liquid, undiluted serum. Immunogen used was full-length recombinant human PDK1. Recognizes the ~60 kDa PDK1 protein in HEK293 cells. Also recognizes ~40 kDa and ~17 kDa unidentified proteins. Suitable for immunoblotting.



Detection of human PDK1 by immunoblotting. Samples: full-length, recombinant human PDK1 (lane 2) and whole cell lysates (40 µg) from HEK293 cells (lane 3). Primary antibody: Anti-PDK1 (1-556) Rabbit pAb (1:3000). Detection: chemiluminescence.

Cat. No. ST1115 **50 µl** **$145**

NEW Recombinant PI 3-Kinases

Name	Cat. No.	Comments	Size	Price
PI 3-Kβ, p100b/p85α, Human Recombinant, *S. frugiperda*	526554	Recombinant, human PI 3-kinase β-isoform. This active complex is suitable for the study of activity regulation and inhibitor screening. *Purity≥90% by SDS-PAGE.*	5 µg	$225
PI 3-Kγ, His•Tag®, Human, Recombinant, *S. frugiperda*	526556	Recombinant, human PI 3-Kinase γ-isoform with a His•Tag® sequence at the N-terminus. This active complex is suitable for studying the regulation of activity and inhibitor screening. *Purity≥95% by SDS-PAGE.*	5 µg	$225
PI 3-Kδ, p110δ/p85α, GST-Fusion, Human, Recombinant, *S. frugiperda*	526558	Recombinant, human PI 3-kinase δ-isoform. The p110δ subunit has a GST sequence for purification of the heterodimer. The active complex is suitable for studying of the regulation of activity and inhibitor screening.	5 µg	$225
PI 3-K NT-frag., His•Tag® fusion	526555	Recombinant, human protein containing the N-terminal 483 aa of human PI 3-kinase (P3C2A, PI 3-K C2α) with one mutation (N483K) expressed in *E. coli* with N-terminal His•Tag® and S•Tag™ sequences. Useful as a substrate for protein tyrosine kinases in *in vitro* assays, but has no intrinsic kinase activity. *Purity: >90% by SDS-PAGE.*	50 µg	$130

Antibodies for PI 3-Kinase Research

Name	Cat. No.	Comments	Size	Price
Anti-PI-3-Kinase Mouse mAb (AB6)	528107	Lyophilized, monoclonal IgG_1, purified. Immunogen used was a recombinant human p85α expressed in *E. coli*. Recognizes the ~ 85 kDa p85α regulatory subunit of PI 3-kinase. Does not cross-react with p85β. Reacts with human, mouse, and rat. **IB, IC, IP**	100 µg	$307
Anti-PI 3-Kinase p110δ, C-Terminal (1026-1044) Rabbit pAb	526553	Liquid, polyclonal IgG, affinity purified. Immunogen used was a synthetic peptide corresponding to a distinct C-terminal region of human PI 3-kinase p110δ, conjugated to KLH. Recognizes a ~110 kDa human PI-3 kinase p110δ protein. **IB, IC**	100 µl	$302
PhosphoDetect™ Anti-PTEN ($pSer^{380}$) Rabbit pAb	ST1072	Liquid, polyclonal IgG, purified. Immunogen used was a synthetic phosphopeptide corresponding to amino acids surrounding the Ser^{380} phosphorylation site of human PTEN. Recognizes the ~54 kDa PTEN protein phosphorylated at Ser^{380}. Reacts with human, mouse, and rat. **IB, IC, IP, PS**	50 µl	$180
PhosphoDetect™ Anti-PDK1 ($pSer^{241}$) Rabbit pAb	ST1073	Liquid, IgG. Immunogen used was a synthetic phosphopeptide corresponding to amino acids surrounding the Ser^{241} phosphorylation site of human PDK1. Recognizes the ~63 kDa PDK1 protein phosphorylated at Ser^{241}. Reacts with human, mouse, and rat. **IB, IC, IP**	50 µl	$180
Anti-SMG1 Rabbit pAb (Anti-PI 3-Kinase-Related Kinase SMG1)	DR1035	Liquid, polyclonal IgG, affinity purified. Immunogen used was a synthetic peptide corresponding to amino acids near the C-terminus of human SMG1. Epitope lies within amino acids 1000-1050. Recognizes the ~340 kDa SMG protein in HeLa cell nuclear extracts. **IB**	50 µg	$145

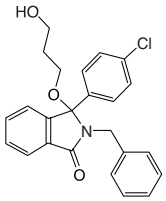
IB: immunoblotting; **IC**: immunocytochemistry; **IP**: immunoprecipitation; **mAb**: monoclonal; **pAb**: polyclonal; **PS**: paraffin sections

NEW Apoptosis Research Products

MDM2 Antagonist III

(2-Benzyl-3-(4-chlorophenyl)-3-(3-hydroxypropoxy)-2,3-dihydroisoindol-1-one)

A cell-permeable isoindolinone compound that binds to MDM2 and disrupts MDM2-p53 interaction (IC_{50} = 15.9 µM). Shown to upregulate p53-dependent luciferase activity and cellular levels of MDM2 and p21 in SJSA cells. *Purity: ≥95% by HPLC.* M.W. 407.9

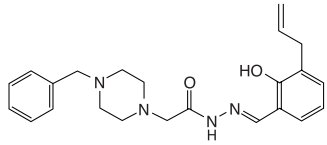


Cat. No. 444149 **10 mg** **$151**

Ref.: Hardcastle, I.R., et al. 2006. *J. Med. Chem.* **49,** 6209; Hardcastle, I.R., et al. 2006. *Bioorg. Med. Chem. Lett.* **15,** 1515.

Procaspase-3 Activator, PAC-1

A cell-permeable activator of procaspase-3 (EC_{50} = 220 nM). Substitution of any of the three aspartate residues in the enzyme's safety-catch region greatly reduces the *in vitro* activation efficiency (EC_{50} = 2.77 µM, 113 µM, and 131 µM for mutant procaspase-3 with DAD, DDA, and ADD sequence, respectively; EC_{50} = 4.5 µM for wild-type procaspase-7 with DTD sequence). Potency of apoptosis induction by PAC-1 in various cells strongly correlates with cellular levels of procaspase-3 expression. *Purity: ≥95% by HPLC.* M.W. 392.5



Cat. No. 529661 **10 mg** **$130**

Ref.: Putt, K.S., et al. 2006. *Nat. Chem. Biol.* **2,** 543.

Gβγ Modulator I, M119

(NSC119910)

A cell-permeable xanthene compound that binds to Gβγ with high affinity (IC_{50} = 200 nM in competition ELISA using biotinylated-$G\beta_1\gamma_2$) and modulates Gβγ interaction with $G\alpha_{i1}$ and GRK2 (IC_{50} = 400 nM and 5 µM, respectively). Shown to block Gβγ-dependent activation of down-stream effectors, PLCβ2, PLCβ3, and PI 3-Kγ, both *in vitro* and *in vivo*. *Purity: ≥95% by HPLC.* M.W. 370.4

Cat. No. 371707 **5 mg** **$115**

Ref.: Bonacci, T.M., et al. 2006. *Science* **312,** 443.

Technical Support
Phone 800 628 8470
E-mail calbiochem@emdchemicals.com

NEW Antibodies for Apoptosis Research

Name	Cat. No.	Comments	Size	Price
Anti-PARC (1-763) Rabbit pAb	DR1040	Liquid, polyclonal IgG, undiluted serum. Immunogen used was a recombinant protein consisting of amino acids 1-763 of human PARC fused to a His•Tag® sequence. Recognizes a ~270 kDa PARC protein in U2OS cells. **IB, IP**	50 µl	$145
Anti-ASC Rabbit pAb	ST1121	Liquid, polyclonal IgG, undiluted serum. Immunogen used was a full-length recombinant human ASC, expressed in *E. coli*. Recognizes the ~21 kDa ASC (apoptosis-associated speck-like protein containing a CARD) protein in HT-29 cells. **IB, IP**	50 µl	$145
Anti-APAF-1 Rabbit pAb	AP1052	Liquid, polyclonal IgG, protein A purified. Immunogen used was a full-length recombinant human APAF-1 fused to a His•Tag® sequence and expressed in *E. coli*. Recognizes the ~130 kDa APAF-1 protein in HeLa cells. **IB**	50 µl	$145

IB: immunoblotting; **IP**: immunoprecipitation; **pAb**: polyclonal

DAPK1, GST-Fusion, Human, Recombinant, *S. frugiperda*

Recombinant, human death associated protein kinase (DAPK1) fused at the N-terminus to a GST-His_6-thrombin cleavage site sequence and expressed in *S. frugiperda* insect cells using a baculovirus expression system. DAPK1 is a Ca^{2+}/calmodulin-dependent serine/threonine kinase that acts as a positive regulator of apoptosis. *Specific activity: ≥50 pmol/min/µg protein. Kinase activity is measured as the molar amount of phosphate incorporated into IAKRRRLSSLRASTSKSESSQK peptide substrate per minute per mg protein at 30°C, using variable concentrations from 0.1 µM to 0.391 µM ATP.*

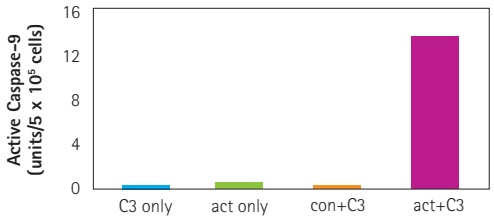
Cat. No. 324782 **10 µg** **$296**

Ref.: Bialik, S. and Kimchi, A., 2006. *Annu. Rev. Biochem.* **75,** 189; Shohat, G., et al. 2001. *J. Biol. Chem.* **276,** 47460; Deiss, L.P., et al. 1995. *Genes Dev.* **9,** 15.

Apoptosis Research Kits

Active Caspase-9 Assay Kit

A 96-well based fluorimetric caspase-9 assay kit that captures active caspase-9 complexed with APAF-1. Active caspase-9 cleaves precursor caspase-3 and activates it, which in turn releases AFC from DEVD-AFC. The fluorescence is measured in a plate reader. Each kit is suitable for up to 480 tests. Suitable for use with human cell lines.

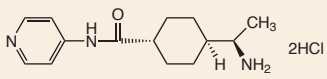


Activated extract and precursor caspase-3 are required for DEVD-AFC cleavage. Caspase-9 in activated and control Jurkat cell extracts (5 x 10^5 cells) were captured in wells coated with caspase-9 capture antibody. Wells were washed and precursor caspase-3 was added and after 60 min. incubation, cleavage of DEVD-AFC by caspase-3 was measured using a fluorescent plate reader. Precursor caspase-3 only (C3 only), activated extracts only (act only), a control extract with precursor caspase-3 (con +C3), and activated extract with precursor caspase-2 (act+C3) were used in this assay. A unit of caspase-9 activity is defined as the amount of active caspase-9 required to activate sufficient caspase-3 to cleave DEVD-AFC at a rate of 1 RFU/minute.

Cat. No. CBA047 **1 kit** **$373**

Y-27632

A highly potent, cell-permeable, selective, ATP-competitive inhibitor of Rho-associated protein kinases (K_i = 140 nM for $p160^{ROCK}$). Also inhibits ROCK-II with equal potency. Blocks dissociation-induced apoptosis in human embryonic stem cells and increase cloning efficiency. *Purity: ≥95% by HPLC.* M.W. 338.3.



Sold under license of U.S. Patent 4,997,834 and PCT Application W098/06,433A1 and under license from Mitsubishi Tanabe Pharma Corporation.

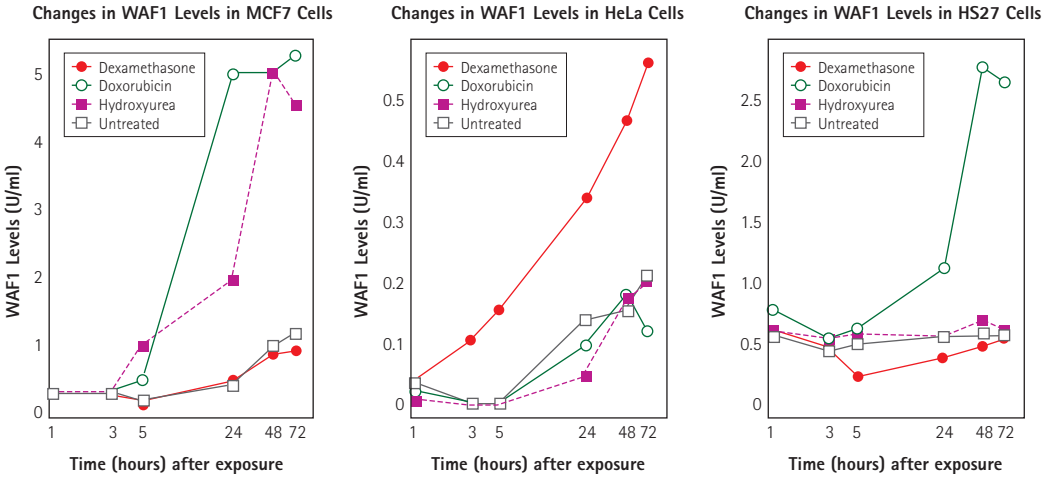
Cat. No. 688000 **1 mg** **$132**
5 mg **$516**

Apoptosis Research Kits *(continued...)*

p21^{WAF1} ELISA Kit

Format: 96-well plate **Sensitivity:** 0.1 U/ml
Assay range: 0.1-20 U/ml **Assay time:** 4 h
Sample type: Cell extracts or tissue culture media

A sandwich ELISA method for assay of WAF1. Suitable for use with human cell line extracts or tissue culture media.



Time, drug, and cell line-dependent changes in WAF1 levels detected by the WAF1 assay. MCF-7, HeLa, and HS27 cells were treated with dexamthasone (1 µM), doxorubicin (0.2 µg/ml), and hydroxyurea (2.5 mM) and tested for WAF1 levels at different time points.

Cat. No. QIA18 **1 kit** **$475**

Live/Dead Double Staining Kit

Assay time: 0.5 h
Sample type: Cell suspensions or adherent cells

This kit is based on fluorescence microscopic detection method and uses a cell-permeable green fluorescent Cyto-dye (*Exc. max.: 488 nm; Em. max.: 518 nm*) to stain live cells, and propidium iodide (*Exc. max.: 488 nm; Em. max.: 615 nm*) to stain dead cells. Stained live and dead cells can be visualized by fluorescence microscopy using a band-pass filter, which detects FITC and rhodamine. Viable cells stain only with the Cyto-dye, fluorescing green, whereas the dead cells stain with both Cyto-dye (green) and propidium iodide (red), resulting in a yellow fluorescence. This kit can be used with a wide range of species. *Optimal staining conditions may vary among different cell types and should be determined empirically by the investigator.*

Cat. No. QIA76 **100 Tests** **$250**

Ref.: Luther, E., and Kamenstsky, L.A. 1996. *Cytometry* **23,** 272; Frey. T., et al. 1995. *Cytometry* **21,** 265.

"As a quality control supervisor, Doug was always hard to please."

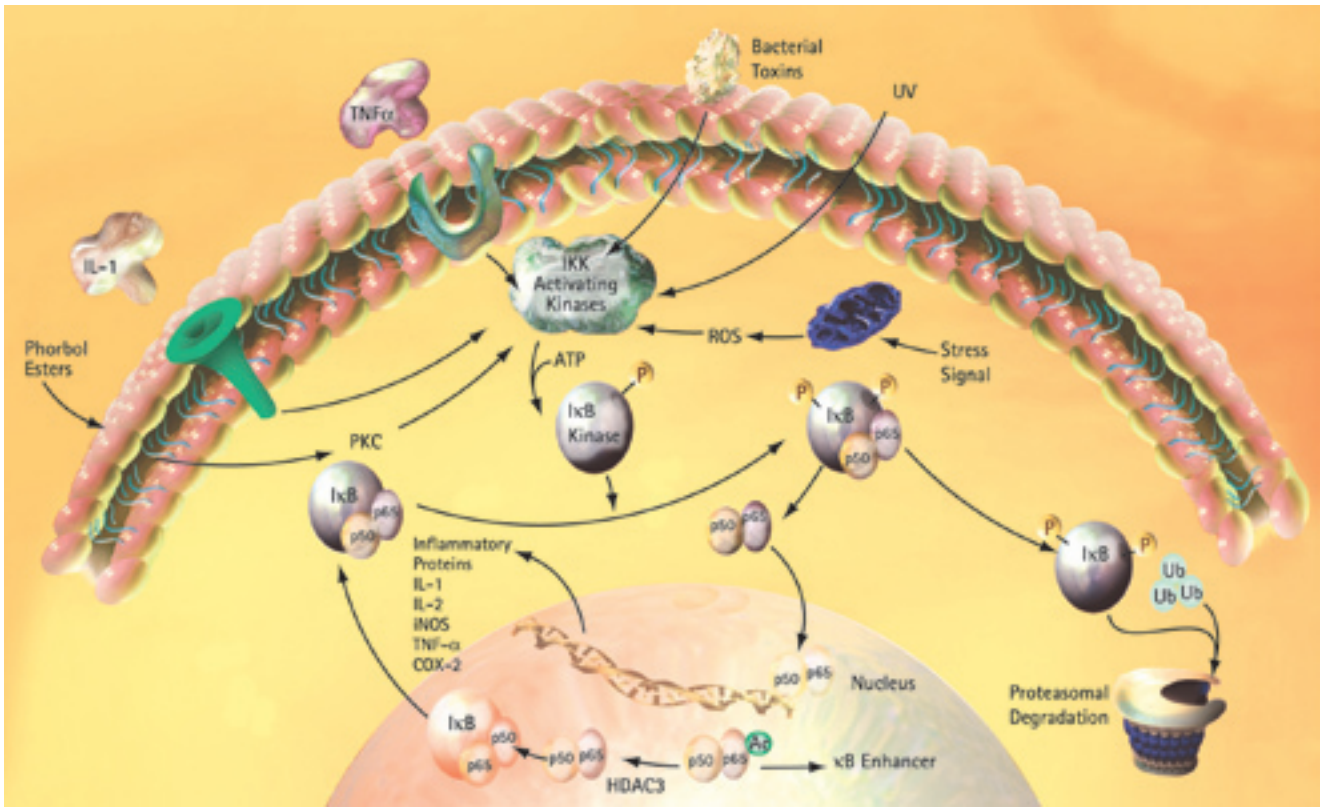
Technical Support
Phone 800 628 8470
E-mail calbiochem@emdchemicals.com

The IKK-NF-κB System: A Target for Inflammation and Cancer

NF-κB is an important regulator of inflammatory and autoimmune responses, cell proliferation, and apoptosis. The activation of NF-κB that occurs via the classical pathway is triggered by bacterial and viral infections and by pro-inflammatory cytokines. Five members of the NF-κB family have been identified: NF-κB1 (p50/p105), NF-κB2 (p52/p100), RelA (p65), RelB, and c-Rel. The p50/RelA (p65) heterodimer is the major Rel/NF-κB complex in most cells. In resting cells, NF-κB is sequestered in the cytoplasm in an inactive form associated with inhibitory molecules, such as IκB. Activation of NF-κB is achieved through the action of IκB kinases (IKK), which phosphorylate IκB and allow its polyubiquitination and degradation by the 26S proteasome complex. This allows the translocation of NF-κB from the cytoplasm to the nucleus where it binds to NF-κB response elements in target genes and regulates their transcription.

In the nucleus, recruitment of NF-κB to its target genes and regulation of NF-κB-mediated transcriptional activation are mediated mainly by phosphorylation and acetylation of NF-κB that enhance its DNA binding activity. Several protein kinases, including PKA, PKC_{ζ}, and casein kinase II directly phosphorylate p65 (at Ser^{276}, Ser^{311}, Ser^{529}, respectively). However, others like PI 3-K/Akt and NF-κB-inducing kinase phosphorylate IKK, which in turn phosphorylates p65 at Ser^{536}. Reversible acetylation of NF-κB can also determine its active or inactive state. p300 and CBP acetyltransferases play a major role in the acetylation of p65, principally targeting $Lys^{218, 221, 310}$. Deacetylation of p65 by histone deacetylase 3 promotes its binding to IκB that leads to rapid export of deacetylated NF-κB from the nucleus into the cytoplasm. One of the target genes activated by NF-κB is that encoding IκBα. Newly synthesized IκBα can enter the nucleus, remove NF-κB from DNA, and export the NF-κB/IκB complex back to the cytoplasm to restore its original latent state.

In most cancer cells NF-κB is constitutively active and resides in the nucleus, which not only protects cancer cells from apoptotic cell death, but may also enhance their growth activity. Hence, designing anti-tumor agents to block NF-κB activity has great therapeutic value. ■



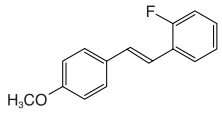
Orders Phone 800 854 3417
Fax 800 776 0999
Web www.emdbiosciences.com/calbiochem

NEW Inhibitors of NF-κB Activation Scheme

NF-κB Activation Inhibitor IV

((E)-2-Fluoro-4'-methoxystilbene)

A cell-permeable trans-stilbene Resveratrol analog that is about 130-fold more potent than Resveratrol in inhibiting TNF-α-stimulated NF-κB reporter activity in 293T cells (IC_{50} = 150 nM). *Purity: ≥98% by HPLC*. M.W. 228.1



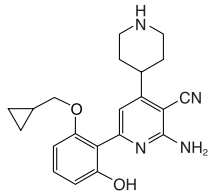
Cat. No. 481412 **10 mg** **$125**

Ref.: Heynekamp, J.J., et al. 2006. *J. Med. Chem.* **49,** 7182.

IKK-2 Inhibitor VIII

(2-Amino-6-(2-(cyclopropylmethoxy)-6-hydroxyphenyl)-4-(4-piperidinyl)-3-pyridinecarbonitrile)

A cell-permeable, selective inhibitor of IKK-2 (IC_{50} = 8.5 and 250 nM for IKK-2 and IKK-1, respectively). Exhibits little effect towards IKK-3, Syk, and MKK4 (IC_{50} > 20 µM). *Purity: ≥95% by HPLC*. M.W. 364.4

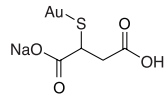


Cat. No. 401487 **1 mg** **$135**

Ref.: Murata, T., et al. 2004. *Bioorg. Med. Chem. Lett.* **14,** 4019.

Aurothiomalate

A gold(I) compound that inhibits the activity of IKK (ID_{50} = 10.9 µM) and disrupts PB1 (Phox and Bem1p) domain-mediated interactions between Par6 and $PKC_ι$ (IC_{50} ~ 1 µM) by modifying cysteine residues within the catalytic domain of IKK and the PB1 domain of $PKC_ι$. Also inhibits $PKC_ι$-dependent Rac1 activation in A549 cells. *Purity: ≥98% (Gold content)*. M.W.368.1



Cat. No. 189401 **50 mg** **$88**

Ref.: Erdogan, E., et al. 2006. *J. Biol. Chem.* **281,** 28450; Stallings-Mann, M., et al. 2006. *Cancer Res.* **66,** 1767; Jeon, K.I., et al. 2000. *J. Immunol.* **164,** 5981; Handel, M.L., et al. 1995. *Proc. Natl. Acad. Sci. USA* **92,** 4497.

Now Available...Ready to Use

InSolution™ NF-κB Activation Inhibitor

A 10 mM (1 mg/281 µl) solution of NF-κB Activation Inhibitor (Cat. No. 481406) in DMSO.

Cat. No. 481407 **1 mg** **$82**

Antibodies for NF-κB Activation Research

Name	Cat. No.	Comments	Size	Price
Anti-NF-κB (p50) (Ab-1) Rabbit pAb	PC136	Liquid, polyclonal IgG, diluted serum. Immunogen used was a synthetic peptide corresponding to amino acids near the N-terminal domain of human NF-κB p50. Recognizes the NF-κB p50 protein in Daudi cells. **ELISA, GS, IB, IP**	20 µl 100 µl	$70 $297
Anti-NF-κB (p65, RelA) (Ab-1) Rabbit pAb	PC137	Liquid, Polyclonal IgG, undiluted serum. Immunogen used was a synthetic peptide corresponding to amino acids near the C-terminal domain of human NF-κB p65 (RelA), conjugated to KLH. Recognizes NF-κB p65 (RelA) protein in Daudi cells. **GS, IB, IP**	20 µl 100 µl	$69 $297
Anti-NF-κB (p65, RelA) (Ab-2) Rabbit pAb	PC138	Liquid, polyclonal IgG. Immunogen used was a a synthetic peptide corresponding to amino acids near the N-terminal domain of human NF-κB p65 (RelA), conjugated to KLH. Recognizes NF-κB p65 (RelA) protein in Daudi cells. **ELISA, GS, IB, IP**	100 µl	$297
Anti-NF-κB (p65) Mouse mAb (2A12A7)	ST1047	Liquid, monoclonal IgG_{2a}, purified. Immunogen used was a recombinant protein containing ~175 amino acids from the C-terminus of human NF-κB p65 (RelA). Recognizes NF-κB p65 (RelA) protein in K562, HeLa, and A431 cells. **ELISA, GS, IB**	100 µl	$240

ELISA: enzyme-linked immunosorbent assay; **GS**: gel-shift; **IB**: immunoblotting; **IP**: immunoprecipitation; **mAb**: monoclonal; **pAb**: polyclonal

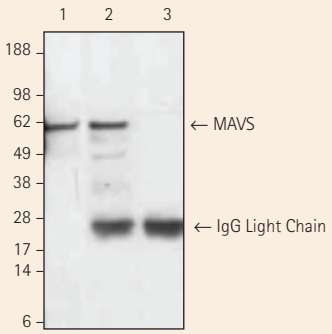
Technical Support
Phone 800 628 8470
E-mail calbiochem@emdchemicals.com

Antibodies for NF-κB Activation Research *(continued...)*

Anti-MAVS Rabbit pAb

Liquid, polyclonal IgG, purified. Immunogen used was a synthetic peptide corresponding to amino acids in middle region of human MAVS. Recognizes the ~56 kDa MAVS protein in Saos-2 cells. MAVS is essential for NF-κB and IRF3 activation by RNA viruses. Suitable for immunoblotting and immunoprecipitation.

Cat. No. ST1116 **50 µg** **$145**



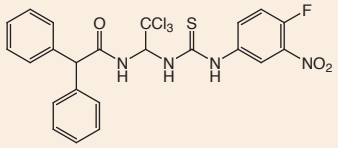
Lane 1: Detection of human MAVS by immunoblotting. Sample: 20 µg of Saos-2 cell lysates. Primary antibody: Anti-MAVS Rabbit pAb (Cat. No. ST1116) (0.1 µg/ml). Detection: chemiluminescence.

Lane 2: Detection of MAVS by immunoprecipitation followed by immunoblotting. Antibody was used at 5 µg/500 µg total protein.

NEW Protein Kinase Inhibitors

Cdk1 Inhibitor IV, RO-3306

A cell-permeable, potent, and ATP-competitive inhibitor of Cdk1 (K_i = 35 nM and 110 nM for Cdk1/B1 and Cdk1/A, respectively). It affects Cdk2/E, PKC_δ, and SGK only at much higher concentrations (K_i = 340, 318, and 497 nM, respectively). *Purity: ≥95% by HPLC.* M.W. 351.5



Cat. No. 217699 **5 mg** **$190**

Ref.: Vassilev, L.T., et al. 2006. Proc. *Natl. Acad. Sci. USA* **103,** 10660.

Cdk/Cyclin Inhibitory Peptide III

(Ac-RWIMYF-NH_2)

A protease resistant, all D-amino acid hexapeptide that selectively binds to a conserved region of cyclin A with high-affinity (K_d ~ 102 nM) and disrupts the formation of Cdk/cyclin complex. Shown to inhibit the kinase activity of Cdk2/cyclin A, Cdk1/cyclin B1 and Cdk6/cyclin D3 (IC_{50} = 1.1 µM, 2.0 µM and 6.4 µM, respectively) in a non-competitive manner with respect to both ATP and protein substrates. Its cell-permeable analog, TAT-NBI1 is also available (Cat. No. 238808). *Purity: ≥97% by HPLC.* M.W. 956.2

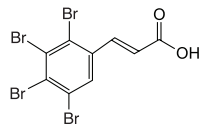
Cat. No. 238807 **5 mg** **$190**

Ref.: Canela, N., et al. 2006. *J. Biol. Chem.* **281,** 35942.

Casein Kinase II Inhibitor III, TBCA

((E)-3-(2,3,4,5-Tetrabromophenyl)acrylic acid)

A cell-permeable, potent, and ATP-competitive inhibitor of Casein Kinase II (IC_{50} = 110 nM, K_i = 77 nM) with greater selectivity than TBB (Cat. Nos. 218697 and 218708) and DMAT (Cat. Nos. 218699 and 218706) against a panel of 28 commonly studied kinases. Shown to induce apoptosis in Jurkat cells (DC_{50} = 7.7 µM). *Purity: ≥95% by HPLC.* M.W. 463.8



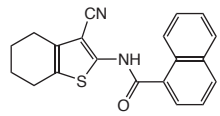
Cat. No. 218710 **5 mg** **$120**

Ref.: Pagano, M.A., et al. 2006. *Chembiochem* **8,** 129.

JNK Inhibitor IX

(N-(3-Cyano-4,5,6,7-tetrahydro-1-benzothien-2-yl)-1-naphthamide

A potent and ATP binding site-targeting inhibitor of JNK2 and JNK3 (pIC_{50} = 6.5 and 6.7, respectively) with little or no activity against JNK1, p38α, and a panel of more than 30 other kinases (pIC_{50} <5.0). *Purity: ≥95% by HPLC.* M.W. 350.4



Cat. No. 420136 **5 mg** **$140**

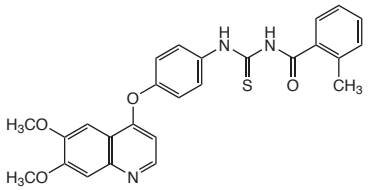
Ref.: Angell, R.M., et al. 2007. *Bioorg. Med. Chem. Lett.* **17,** 1296.

NEW Protein Kinase Inhibitors *(continued...)*

PDGF Receptor Tyrosine Kinase Inhibitor V

(N-(4-((6,7-Dimethoxy-4-quinoyl)oxy)phenyl)-N'-(2-methylbenzoyl)thiourea)

A cell-permeable, potent, ATP-competitive, and reversible inhibitor of PDGFR tyrosine kinase activity (IC_{50} = 4 and 7.6 nM in ligand-induced cellular PDGFR phosphorylation and in *in vitro* kinase activity, respectively). Inhibits c-kit receptor only at much higher concentrations (IC_{50} = 434 and 234 nM in receptor phosphorylation and kinase activity, respectively). *Purity:* ≥*95% by HPLC*. M.W. 527.6



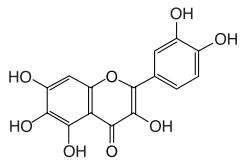
Cat. No. 521234 **1 mg** **$165**

Ref.: Furuta, T., et al. 2006. *J. Med. Chem.* **49,** 2186.

Quercetagetin

(3,3',4',5,6,7-Hexahydroxyflavone)

A cell-permeable flavanol compound that acts a potent, ATP-competitive, and reversible inhibitor of PIM1 kinase (IC_{50} = 340 nM). Exhibits ≥7-fold selectivity over 8 other kinases tested, including PIM2 (IC_{50} = 3.45 µM). Shown to induce growth arrest (ED_{50} = 3.8 µM) in PIM1-expressing RWPE2 cells. *Purity:* ≥*95% by HPLC*. M.W. 318.3



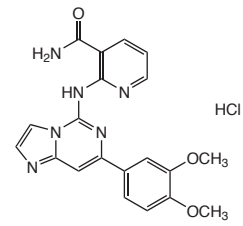
Cat. No. 551590 **5 mg** **$230**

Ref.: Holder, S., et al. 2007. *Mol. Cancer Ther.* **6,** 163.

Syk Inhibitor IV, BAY 61-3606

(2-(7-(3,4-Dimethoxyphenyl)-imidazo[1,2-c]pyrimidin-5-ylamino)-nicotinamide, HCl)

A cell-permeable, potent, ATP-competitive, reversible, and highly selective inhibitor of Syk tyrosine kinase (IC_{50} = 10 nM) with no inhibitory effect against Btk, Fyn, Itk, Lyn, and Src even at concentrations as high as 4.7 µM. *Purity:* ≥*97% by HPLC*. M.W. 462.9



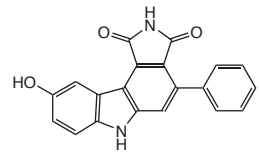
Cat. No. 574714 **2 mg** **$135**

Ref.: Yamamoto, N., et al. 2003. *J. Pharm. Exp. Ther.* **306,** 1174.

Wee1/Chk1 Inhibitor

(6-Butyl-4-(2-chlorophenyl)-9-hydroxypyrrolo[3,4-c]carbazole-1,3-(2H,6H)-dione)

A potent, ATP-competitive inhibitor of Wee1 and Chk1 (IC_{50} = 97 and 47 nM, respectively). *Purity:* ≥*95% by HPLC*. M.W. 346.3



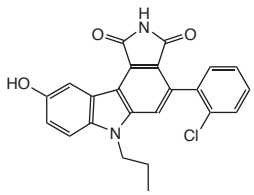
Cat. No. 681637 **1 mg** **$120**

Ref.: Palmer, B.D., et al. 2006. *J. Med. Chem.* **49,** 4896; Squire, C.J., et al. 2005. *Structure* **13,** 541.

Wee1 Inhibitor II

(6-Butyl-4-(2-chlorophenyl)-9-hydroxypyrrolo[3,4-c]carbazole-1,3-(2H,6H)-dione)

A potent, ATP-binding site-targeting inhibitor of Wee1 (IC_{50} = 59 nM) with a ~590-fold selectivity over the related checkpoint kinase Chk1 (IC_{50} = 35 µM). *Purity:* ≥*97% by HPLC*. M.W. 418.9



Cat. No. 681641 **1 mg** **$140**

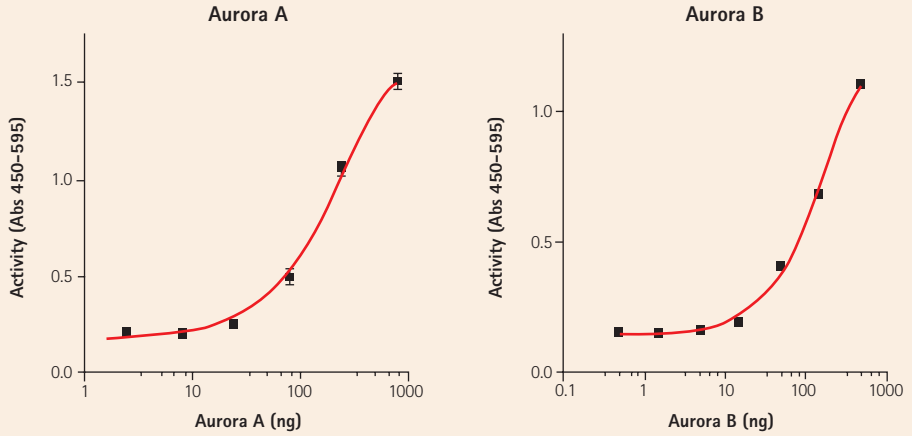
Ref.: Palmer, B.D., et al. 2006. *J. Med. Chem.* **49,** 4896.

NEW Protein Kinase Activity Kit

K-LISA™ Aurora Kinase Activity Kit

Format: 96-well plate
Sensitivity: 16 ng for Aurora A; 11 ng for Aurora B
Assay range: 20-1000 ng
Sample type: Purified enzyme or enzyme immunoprecipitated from cell lysates

An ELISA-based activity assay kit for for measuring the kinase activity of purified or partially purified Aurora A and Aurora B, *in vitro* Aurora A and Aurora B inhibitor screening, and for assessing the regulation of Aurora A and Aurora B in cell signaling. This kit utilizes a biotinylated peptide substrate (ARTKQTARKSTGGKAPRKQLA-GGK-biotin) that is phosphorylated on serine by Aurora A and Aurora B. The phosphorylated substrate is detected with the Phospho-Histone H3 Antibody, followed by HRP-Antibody Conjugate and color development with TMB Substrate.



The activity of Aurora A, Human, Recombinant, His•Tag® (Cat. No. 481413) (1.66-1660 ng) and Aurora B (0.5-500 ng) was determined. Assay range: 20-1000 ng

Cat. No. CBA051 **1 kit** **$365**

NEW Aurora A, His•Tag®, Human Rec., *S. frugiperda*

A full-length, recombinant, human Aurora A kinase (amino acids 2-403; Accession: NM_003600) fused at the N-terminus to a His•Tag® sequence and expressed in Sf9 insect cells using a baculovirus expression system. *Specific activity: ≥120 U/µg protein. One unit is defined as the amount of enzyme that will phosphorylate 1 pmol of Ser/Thr 1 peptide substrate per min at 30°C, pH 7.4. Purity: ≥90% by SDS-PAGE.* M.W. 50,000.

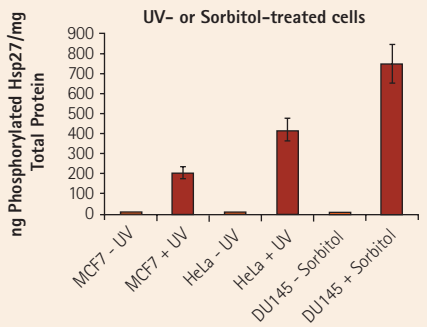
Cat. No. 481413 **10 µg** **$265**

PhosphoDetect™ Hsp27 (pSer$^{78/82}$) ELISA Kit

Format: 96-well plate
Assay range: 0.1-10 ng/ml; Assay time: 4.5 h

A quantitative sandwich ELISA for assay of Hsp27 phosphorylated at Ser^{78} and Ser^{82}. Suitable for use with cell lysates, tissue extracts, and biological fluids. The assay utilizes an Hsp27-specific monoclonal antibody, immobilized on the wells of a 96-well plate to capture Hsp27.

Cat. No. CBA078 **1 kit** **$495**

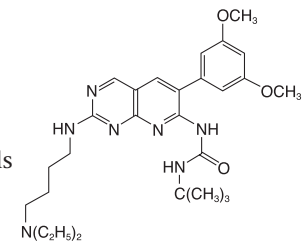


NEW Recombinant Protein Kinases

Name	Cat. No.	Comments	Size	Price
CDK1/CycB, GST-Fusion, Human, Recombinant, *S. frugiperda*	325897	Recombinant, human Cdk1 (amino acids 1-297) and recombinant human cyclin B (amino acids 1-433), each fused to a GST-His_6-thrombin cleavage site sequence at their respective N-termini and co-expressed in *S. frugiperda* using a baculovirus expression system. M.W. Cdk1 = 63,882 Da; M.W. cyclin B = 78, 925 Da. *Specific activity:≥2 pmol/min/µg protein.*	10 µg	$285
CDK2/CycA, GST-Fusion, Human, Recombinant, *S. frugiperda*	325898	Recombinant, human CDK2 (amino acids 1-298) and recombinant, human cyclin A (amino acids 1-432), each fused to a GST-thrombin cleavage site sequence at their respective N-termini and co-expressed in *S. frugiperda* using a baculovirus expression system. M.W. CDK2 = 60,200 Da; M.W. cyclin A = 74,900 Da. *Specific activity:≥9 pmol/min/µg protein.*	10 µg	$285
CDK4/CycD1, GST-Fusion, Human, Recombinant, *S. frugiperda*	325899	Recombinant, human CDK4 and recombinant, human cyclin D1, each fused to a GST-thrombin cleavage site sequence at their respective N-termini and co-expressed in *S. frugiperda* using a baculovirus expression system. M.W. CDK4 = 59,700 Da; M.W. cyclin D1 = 60,000 Da. *Specific activity:≥91 pmol/min/µg protein.*	10 µg	$285
CDK6/CycD1, GST-Fusion, Human, Recombinant, *S. frugiperda*	325900	Recombinant, human CDK6 and recombinant, human cyclin D1, each fused to a GST-thrombin cleavage site sequence at their respective N-termini and co-expressed in *S. frugiperda* using a baculovirus expression system. M.W. CDK6 = 63,300 Da; M.W. cyclin D1 = 60,000 Da. *Specific activity:≥11 pmol/min/µg protein.*	10 µg	$285
NEK2, GST-Fusion, Human, Recombinant, *S. frugiperda*	325888	Recombinant, human Never in mitosis gene A-related protein kinase 2 (NEK2) fused at the N-terminus to a GST-His_6-thrombin cleavage site sequence and expressed in *S. frugiperda* using a baculovirus expression system. NEK2 is a member of a serine/threonine-protein kinase family that plays an important role in mitotic regulation. *Specific activity:≥15 pmol/min/µg protein.*	10 µg	$296
PAK1, GST-Fusion, Human, Recombinant, *S. frugiperda*	325889	Recombinant, human p21-activated protein kinase 1 fused at the N-terminus to a GST-His_6-thrombin cleavage site sequence and expressed in *S. frugiperda* using a baculovirus expression system. *Specific activity:≥325 pmol/min/µg protein.*	10 µg	$296
WEE1, GST-Fusion, Human, Recombinant, *S. frugiperda*	325896	Recombinant, human WEE1 fused at the N-terminus to a GST-His_6-thrombin cleavage site sequence and expressed in *S. frugiperda* using a baculovirus expression system. *Specific activity:≥1 pmol/min/µg protein.*	10 µg	$285

NEW Inhibitors for Angiogenesis Research

FGF/VEGF Receptor Tyrosine Kinase Inhibitor, PD173074



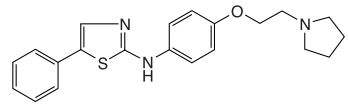
A cell-permeable, potent, ATP-competitive, and reversible inhibitor of FGF and VEGF receptor tyrosine kinaes (IC_{50} = 21.5 nM for FGFR1). It inhibits PDGFR and c-Src kinases only at much higher concentration (IC_{50} = 17.6 µM, 19.8 µM, respectively). Blocks the autophosphorylation of endogenous FGFR1 (IC_{50} <5 nM) and overexpressed VEGFR2 (IC_{50} <200 nM) in NIH-3T3 cells *in vitro*, and FGF- and VEGF-induced angiogenesis in mice *in vivo*. *Purity: ≥97% by HPLC.* M.W. 523.7

Cat. No. 341607 **2 mg** **$125**

Ref.: Koziczak, M., et al. 2004. *Oncogene* **23,** 3501; Trudel, S., et al. 2004. *Blood* **103,** 3521; Skaper, S.D., et al. 2000. *J. Neurochem.* **75,** 1520; Mohammadi, M., et al. 1998. *EMBO J.* **17,** 5896.

Flt3 Inhibitor III

(5-Phenyl-N-(4-(2-(1-pyrrolidinyl)ethoxy)phenyl)-2-thiazolamine)



A cell-permeable, potent, ATP binding site-targeting inhibitor of Flt3 (IC_{50} = 50 nM). It inhibits c-Kit, KDR, c-Abl, Cdk1, c-Src, and Tie-2 only at much higher concentrations (IC_{50} = 0.26, 0.91, 1.2, 2.1, 2.8, and 8.0 µM, respectively). Blocks Flt3-dependent cell proliferation in a dose-dependent manner. *Purity: ≥95% by HPLC.* M.W. 365.5

Cat. No. 343022 **5 mg** **$155**

Ref.: Furet, P., et al. 2006. *J. Med. Chem.* **49,** 4451.

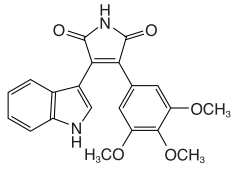
Technical Support
Phone 800 628 8470
E-mail calbiochem@emdchemicals.com

NEW Inhibitors for Angiogenesis Research *(continued...)*

VEGF Receptor 2/3 Tyrosine Kinase Inhibitor

(3-(Indole-3-yl)-4-(3,4,5-trimethoxyphenyl)-1H-pyrrole-2,5-dione)

A cell-permeable, potent and ATP-competitive inhibitor of VEGFR-2 and -3 tyrosine kinase (IC_{50} = 2.5 nM and 5 nM, respectively) with >100-fold selectivity over 25 other commonly studied kinases. Exhibits excellent *in vivo* anti-angiogenic efficacy in chick embryo assay. *Purity: ≥97% by HPLC.* M.W. 378.4



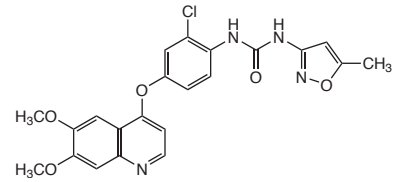
Cat. No. 676499 **5 mg** **$160**

Ref.: FPeifer, C., et al. 2006. *J. Med. Chem.* **49,** 7549; Peifer, C., et al. 2006. *J. Med. Chem.* **49,** 1271

VEGF Receptor Tyrosine Kinase Inhibitor IV

(N-(2-Chloro-4-((6,7-dimethoxy-4-quinolyl)oxy)phenyl)-N'-(5-methyl-3-isoxazolyl)urea)

A cell-permeable, potent pan-VEGFR tyrosine kinase inhibitor (IC_{50} = 30 nM, 6.5 nM and 15 nM for VEGFR-1, 2, and 3, respectively). Also inhibits the activity of EphB2, PDGFR-α, PDGFR-β, c-Kit and Tie-2 (IC_{50} = 24 nM, 40 nM, 49 nM, 78 nM and 78 nM, respectively). *Purity: ≥95% by HPLC.* M.W. 472.9.



Cat. No. 676483 **500 µg** **$125**

Ref.: Nakamura, K., et al. 2006. *Cancer Res.* **66,** 9134.

Proteins for Angiogenesis Research

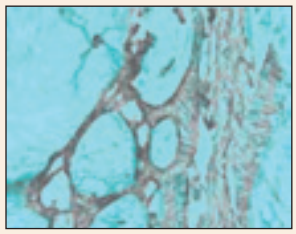
Name	Cat. No.	Comments	Size	Price
Endostatin Protein, Human, Recombinant, *Pichia pastoris**	324768	Recombinant, human endostatin expressed in and purified from *Pichia pastoris.* A ~20 kDa C-terminal fragment of collagen XVIII that acts as a potent inhibitor of angiogenesis and tumor growth in vitro and in vivo. *Biological activity: 10 µg/ml endostatin will inhibit 50% tube formation in the presence of 10 ng/ml VEGF and 70% tube formation in the presence of 5 ng/ml bFGF.*	250 µg 1 mg	$235 $613
Endostatin Protein, Mouse, Recombinant, *Pichia pastoris**	324769	Recombinant, mouse endostatin. A ~20 kDa C-terminal fragment of collagen XVIII that acts as a potent inhibitor of angiogenesis and tumor growth *in vitro* and *in vivo. Biological activity: 3 µg/ml endostatin will inhibit 50% tube formation.*	250 µg 1 mg	$222 $591
Flt-3, GST-Fusion, Human, Recombinant, *S. frugiperda*	325880	Recombinant, human Flt-3 fused at the N-terminus to a GST-His_6-thrombin cleavage site sequence and expressed in *S. frugiperda* insect cells using a baculovirus expression system. *Specific activity:≥25 pmol/min/µg protein.*	10 µg	$296
TIE2, GST-Fusion, Human, Recombinant, *S. frugiperda*	325894	Recombinant, human tunica interna endothelial cell kinase 2 (TIE2) fused at the N-terminus to a GST-His_6-thrombin cleavage site sequence and expressed in *S. frugiperda* insect cells using a baculovirus expression system. *Specific activity:≥95 units/µg protein.*	10 µg	$285
VEGF-R1, GST-Fusion, Human, Recombinant, *S. frugiperda*	325895	Recombinant, human VEGF-R1 fused at the N-terminus to a GST-His_6-thrombin cleavage site sequence and expressed in *S. frugiperda* insect cells using a baculovirus expression system. *Specific activity:≥45 pmol/min/µg protein.*	10 µg	$285

* Sold under license of U.S. Patents 6,764,995; 6,746,865; and corresponding patents.

PhosphoDetect™ Anti-VEGF Receptor 2/3 (pAb-1) Rabbit pAb

Liquid, polyclonal IgG, undiluted serum. Immunogen used was a a synthetic phosphopeptide [GLARDIpYKDPDpYVRKGD(C)] corresponding to amino acids in human VEGF Receptor 2/3. Recognizes phosphorylated VEGF receptor 2/3 in human cells. Suitable for immunoblotting and paraffin sections.

Cat. No. PC460 **25 µl** **$255**



Proteins for Angiogenesis Research *(continued...)*

VEGF ELISA Kit, Human

Sensitivity: 5.0 pg/ml
Assay range: 32.2-1000 pg/ml
Assay time: 4.5 h

A 96-well plate sandwich ELISA assay for human VEGF. Suitable for use with cell culture media, plasma, and serum. Detects both natural and recombinant human VEGF.

Cat. No. QIA51 **1 kit** **$515**

Sample Type	Average% Recovery	Range
Cell Culture Media (n=5)	102	95-111%
Serum (n=5)	102	92-115%
EDTA Plasma (n=5)	97	82-113%
Heparin Plasma (n=5)	93	82-102%
Citrate Plasma (n=5)	100	88-113%

The average recovery of VEGF protein, spiked to three levels in five samples is shown

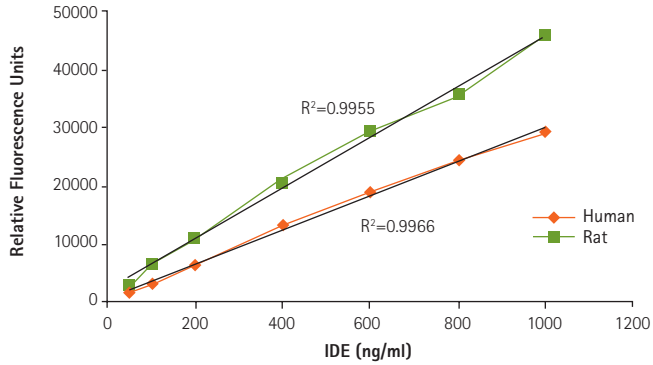
NEW Research Tools for Diabetes Research

Innozyme Insulysin/IDE Immunocapture Activity Assay Kit

Format: 96-well plate
Detection method: Fluorescence
Assay range: 50-1000 ng/ml
Sample type: cell lysates, tissue extracts, and biological fluids

A specific and sensitive assay kit for measuring active insulysin (IDE) from human, mouse, or rat samples. This kit employs an affinity-purified polyclonal antibody immobilized on a 96-well plate to capture IDE. Activity of captured IDE is measured using a FRET substrate, Mca-GGFLRKHGQ-EDDnp. Substrate is cleaved between R and K , which relieves the internal quenching. *(Exc. max. 320 nm; Em. max. 405 nm).*

Cat. No. CBA079 **1 kit** **$525**



Recombinant rat and human IDE was measured using the InnoZyme™ Insulysin/IDE Immunocapture Activity Assay Kit (Cat. No. CBA079). Incubation period: 4 hours at 37˚C.

Product	Cat. No.	Comments	Size	Price
Insulin Degrading Enzyme, His•Tag®, Rat, Recombinant, *S. frugiperda*	407241	A metalloprotease that degrades insulin and a variety of other peptides including amyloid peptides. *Specific activity:≥4 U/mg protein. Purity:≥90% by SDS-PAGE.*	50 µg	$191
Anti-IDE/Insulysin Rabbit pAb	ST1120	Polyclonal IgG, purified. Immunogen: a synthetic peptide corresponding to amino acids at the N-terminus of human IDE/insulysin. Recognizes the ~110 kDa IDE protein in HT1080 cells. Reacts with human. **IB, IP**	50 µg	$145
Anti-IDE, N-Terminal (97-273) Rabbit pAb	PC730	Polyclonal IgG, undiluted serum. Immunogen: a recombinant protein containing amino acids 97-273 of rat IDE fused to GST. Recognizes the ~115 kDa endogenous and recombinant IDE. Reacts with hamster, human, mouse, rat. **ELISA, IB, IC**	100 µl	$289

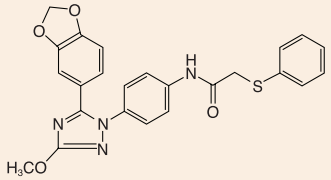
ELISA: enzyme-linked immunosorbent assay; **IB**: immunoblotting; **IC**: immunocytochemistry; **IP**: immunoprecipitation; **pAb**: polyclonal

Technical Support
Phone 800 628 8470
E-mail calbiochem@emdchemicals.com

SecinH3

(N-(4-(5-(1,3-Benzodioxol-5-yl)-3-methoxy-1H-1,2,4-triazol-1-yl)phenyl)-2-(phenylthio)acetamide)

A cell-permeable inhibitor of Sec7-specific GEFs (guanine nucleotide exchange factors) activity that also blocks insulin signaling pathway. Shown to selectively inhibit pIRS-1 by IR and display insulin resistance in mouse model. *Purity: ≥98% by HPLC.* M.W. 460.5



Cat. No. 565725 **5 mg** **$185**

Ref.: Hafner, M., et al. 2006. *Nature* **444,** 941. Fuss, B., et al. 2006. *Nature* **444,** 945.

AMPK, His•Tag®, Human, Recombinant, *S. frugiperda*

Full length recombinant AMPK subunits (A1, B1, and G1) with C-terminal His•Tag® fusions coexpressed in Sf9 insect cells. AMPK is involved in sensing energy levels in the cell due to changes in AMP levels. *Specific activity: ≥2755 nmol/min/mg. Purity: ≥95% by SDS-PAGE.*

Cat. No. 171536 **5 µg** **$195**

Ref.: Scott, J.W., 2007. *EMBO J.* **26,** 806; Minokoshi, Y et al. 2004. *Nature* **428,** 569.

p70S6K, Human, Recombinant, *S. frugiperda*

A full-length, active, recombinant, human p70S6 kinase. *Activity: Kinase activity is measured as the amount of radioactivity incorporated into S6K substrate peptide (CKRRRLASLR) at 30˚C, using a final concentration of 50 µM [^{32}P] ATP. Purity: ≥75% by SDS-PAGE.* M.W. 76,000

Cat. No. 506182 **5 µg** **$337**

Ref.: Scott, J.W., 2007. *EMBO J.* **26,** 806; Minokoshi, Y et al. 2004. *Nature* **428,** 569.

FKBP12, GST-Fusion, Human, Recombinant, *E. coli*

A full-length recombinant, human FK506 binding protein 12-rapamycin associated protein 1 (FKBP12) fused to GST at the N-terminus and expressed in *E. coli*. FKBP12 is a cytosolic receptor for both rapamycin and FK506 that also serves as a natural cofactor for rapamycin inhibition of mTOR. *Purity: ≥90% by SDS-PAGE.* M.W. 12,000

Cat. No. 325902 **60 µg** **$205**

Ref.: Jin, Y.J., et al. 1991. *Proc. Natl. Acad. Sci. USA* **88,** 6677.

Stem Cell Marker Antibodies

Stem cells have the unique ability to self-renew and generate additional stem cells as well as to differentiate into various progenitor cells in response to appropriate signals. They are classified as either embryonic stem cells (ES) or adult stem cells (tissue-specific stem cells). ES are derived from the inner cell mass of preimplantation embryos and are considered to be the most pluripotent stem cell population. They can undergo infinite, undifferentiated proliferation *in vitro* and can also differentiate into a wide variety of somatic and extra-embryonic tissues. Adult stem cells, unspecialized cells found in differentiated tissues, can self-renew and differentiate into mature cell types of the specific tissue.

Some advances have been made in the isolation and characterization of adult stem cells. However, tagging and identifying these cells is a challenging task. Fortunately, each cell type has a certain combination of receptors on their surface that makes them distinguishable from other cells. Researchers use this biological uniqueness of stem cell receptors and their chemical properties to "tag" and identify these cells and sort them by FACS or visualize them under a microscope followed by fluorescent tagging.

Name	Cat. No.	Comments	Size	Price
Anti-BMI1 (1-326) Rabbit pAb	AP1050	Liquid, polyclonal IgG, undiluted serum. Immunogen used was a full-length recombinant human BMI-1 protein (amino acids 1-326). Recognizes the ~44 kDa BMI protein in U2OS cells. **IB**	50 µl	$145
Anti-Nestin Rabbit pAb	ST1117	Liquid, polyclonal IgG, purified. Immunogen used was a synthetic peptide corresponding to amino acids from an internal region of human NES. Recognizes the ~220 kDa Nestin protein in SHSY-5Y cells. **IB, IP**	50 µg	$145
Anti-Nestin Mouse mAb (2C13B9)	ST1111	Liquid, monoclonal IgG_1, purified. Immunogen used was a a GST fusion protein containing amino acids 1464-1614 of human nestin. Recognizes the ~220-240 kDa Nestin protein in U251 cells. **FS, IB, IC**	100 µl	$244
Anti-Nanog Rabbit pAb	SC1000	Liquid, polyclonal IgG, purified. Immunogen used was a synthetic peptide corresponding to amino acids within residues 1-50 of mouse Nanog. Recognizes the ~40 kDa Nanog protein in mouse myeloid and embryonic stem cells. **IB, IP**	50 µg	$145
Anti-CD117 Mouse mAb (57A5)	218150	Liquid, monoclonal IgG_1, purified. Immunogen used was human MO7e tumor cells. Recognizes the ~150 kDa CD117 protein in human cells. **FC, FS, IP**	100 µg	$264
Anti-CD34 Mouse mAb (QBEnd/10)	OP164	Liquid, monoclonal IgG_1, purified. Immunogen used was detergent-solubilized vesicular suspension prepared from a perfusate of human term placenta. Recognizes CD34 selectively expressed on human lymphoid and myeloid hematopoietic progenitor cells and on vascular endothelial cells in normal tissues and benign and malignant proliferations. **FC, PS**	100 µg	$255
Anti-Pax3 Rabbit pAb	CA1010	Liquid, polyclonal IgG, undiluted serum. Immunogen used was a recombinant protein containing amino acids 1-347 of human Pax3 fused to GST. Recognizes the ~56 kDa Pax3 protein, the ~97 kDa Pax3-FHKR fusion protein, and possibly other Pax3 splice variants. **IB, IC**	50 µl	$268
Anti-Pax-5 (1-15) Rabbit pAb	PC700	Liquid, polyclonal IgG, purified. Immunogen used was a synthetic peptide (MDLEKNYPTPRTSRT) corresponding to amino acids 1-15 of human Pax-5. Recognizes the ~50 kDa Pax-5 protein in Raji cell nuclear extracts. **ELISA, IB**	100 µl	$307
Anti-BMP-1 (Ab-1) Rabbit pAb	PC571	Liquid, polyclonal IgG, purified. Immunogen used was a synthetic peptide corresponding to amino acids at the N-terminus of human BMP-1. Recognizes the ~97-110 kDa BMP-1 protein in culture medium from TPA-treated fibroblasts. **IB**	50 µg	$204
Anti-BMP-2/4, C-Terminal Rabbit pAb	203640	Liquid, polyclonal IgG. Immunogen used was a synthetic peptide corresponding to the last 20 amino acids at the C-terminus of human BNP-2/4. Recognizes the ~18 kDa (reducing conditions) BMP-2 and BMP-4 proteins. **ELISA, IB, IP**	100 µg	$290
Anti-BNF1 (150-250) Rabbit pAb	CA1021	Liquid, polyclonal IgG, purified. Immunogen used was a synthetic peptide corresponding to amino acids within residues 150-250 of human BNF1. Recognizes the ~50 kDa BNF1 protein in DU145 cells. **IB**	50 µg	$139

ELISA: enzyme-linked immunosorbent assay; **FC**: flow cytometry; **FS**: frozen sections; **IB**: immunoblotting; **IC**: immunocytochemistry; **IP**: immunoprecipitation; **mAb**: monoclonal; **pAb**: polyclonal; **PS**: paraffin sections

Technical Support
Phone 800 628 8470
E-mail calbiochem@emdchemicals.com

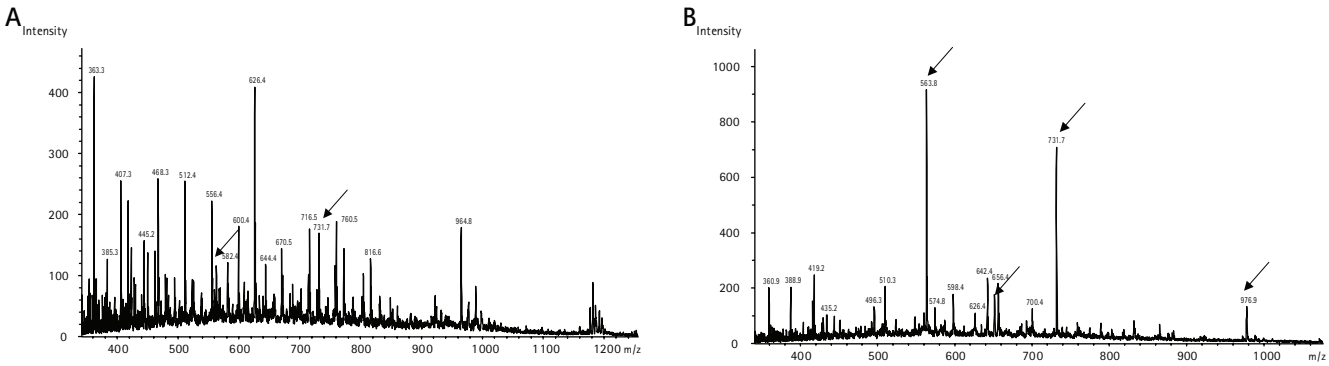
Modulators of Stem Cell Differentiation

Name	Cat. No.	Comments	Size	Price
Cardiogenol C	217460	A cell-permeable pyrimidine compound that potently induces the differentiation of embryonic stem cells into cardiomyocytes (EC_{50} = 100 nM). *Purity:≥95% by HPLC.*	5 mg	$148
Cyclopamine, *Veratrum californicum*	239803	A natural alkaloid isolated that acts as a specific Sonic Hedgehog signaling antagonist. Acts at the level of Smoothened (Smo). *Purity:≥97% by HPLC.*	1 mg	$126
Cyclopamine-KAAD	239804	A potent analog of Cyclopamine (Cat. No. 239803) that specifically inhibits the Hedgehog (Hh) signaling with similar or lower toxicity (IC_{50} = 20 nM in Shh-LIGHT2 assay; 50 nM in $p2^{Ptch-/-}$cells; 500 nM in SmoA1-LIGHT cells). Binds to SmoA1 and promotes its exit from the endoplasmic reticulum. Suppresses both the ShhNp-induced pathway activity and SmoA1-induced reporter activity. *Purity:≥95% by TLC.*	100 µg	$137
Jervine	420210	A cell-permeable steroidal alkaloid similar to cyclopamine (Cat. No. 239803) that blocks Sonic Hedgehog signaling (IC_{50} ~ 500 - 700 nM in s12 cells). *Purity:≥98% by TLC.*	1 mg	$99
Purmorphamine	540220	A cell-permeable purine compound that induces osteoblast differentiation of multipotent mesenchymal progenitor cells C3H10T1/2 (EC_{50} = 1 µM) and lineage-commited preosteoblasts MC3T3-E1. Its effect can be synergized with that of bone morphogenetic protein-4. *Purity:≥98% by HPLC.*	5 mg	$148
Reversine	554717	A cell-permeable purine analog that acts as a dedifferentiation-inducing agent. Shown to induce mouse C2C12 myoblast cells to become multipotent mesenchymal progenitor cells in the concentration range of 1 - 10 µM. *Purity:≥95% by HPLC.*	5 mg	$148
SANT-1	559303	A potent antagonist of the Sonic Hedgehog signaling pathway (IC_{50} = 20 nM in the Shh-LIGHT2 assay and in $Ptch1^{-/-}$ cells] by binding directly to Smoothened (Smo; K_d = 1.2 nM). *Purity:≥95% by HPLC.*	5 mg	$113
Stem Cell Proliferation Inhibitor	569620	A tetrapeptide (Ac-SDKP) that acts as a natural inhibitor of pluripotent hematopoietic stem cell proliferation. Protects bone marrow against chemotherapeutic agents, ionizing radiations, hyperthermia, or phototherapy-induced toxicity. *Purity:≥97% by HPLC.*	5 mg	$133
Stem Cell Factor, Human, Recombinant, *E. coli*	569600	A hematopoietic growth factor that stimulates the growth of cells of multiple lineage. *Biological activity: ED_{50} = 2.5 - 5.0 ng/ml as measured in a cell proliferation assay using a factor-dependent human erythroleukemic cell line. Purity:≥95% by SDS-PAGE.*	10 µg	$356
Stem Cell Factor, Mouse, Recombinant, *E. coli*	569610	A hematopoietic growth factor. *Biological activity: ED_{50} = 5.0 - 10.0 ng/ml as measured in a cell proliferation assay using a factor-dependent human erythroleukemic cell line. Purity:≥95% by SDS-PAGE.*	10 µg	$356

NEW Kits for your Proteomics Research

ProteoExtract® Phosphopeptide Enrichment SCIMAC Kit

The ProteoExtract® Phosphopeptide Enrichment SCIMAC Kit is a useful tool for enrichment of phosphorylated peptides from complex samples by combination of strong cation exchange chromatography (SCX) and immobilized metal ion affinity chromatography (IMAC). The identification of phosphorylation sites is accomplished by mass spectrometry. Captured and eluted phosphopeptide fractions are ready for MALDI- and ESI- mass spectrometry analysis.



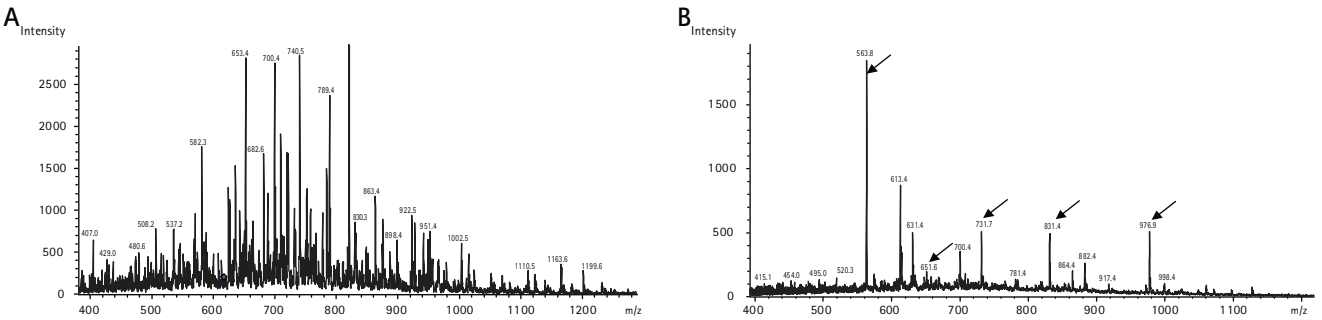
The combination of SCX and IMAC exhibits high selectivity for phosphopeptides by reducing non-specific binding of peptides from complex mixtures. A complex peptide mixture derived from a tryptic digest of porcine liver extract was spiked with α-casein and two synthetic phosphopeptides. The samples were subsequently processed using (A) an iron oxide-based IMAC material alone or (B) the combination of SCX with zirconium-based IMAC particles. Mass spectrometry analysis was performed using ESI-LC/MS equipment operated in positive mode.

Cat. No. 539723 **1 kit** **$275**

NEW Kits for your Proteomics Research *(continued...)*

ProteoExtract® Phosphopeptide Enrichment TiO_2 Kit

The ProteoExtract® Phosphopeptide TiO_2 Enrichment Kit is designed for enrichment of phosphorylated peptides from complex samples by a highly selective titanium oxide solid phase. It enhances the ability to routinely identify and characterize large numbers of phosphorylated species within complex protein mixtures taking advantage of a novel titanium dioxide material. Captured and eluted phosphopeptide fractions are ready for MALDI- and ESI- mass spectrometry analysis.



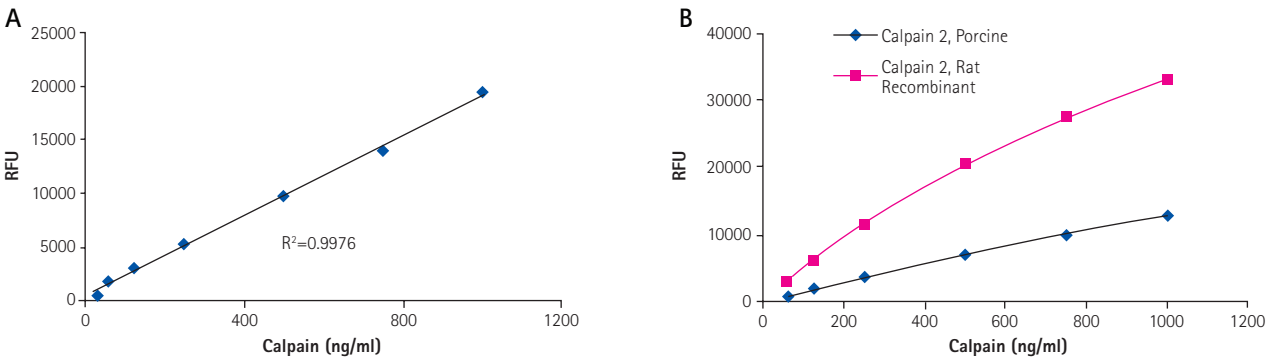
The activity of titanium dioxide allows for selective and sensitive phosphopeptide enrichment with low background from complex mixtures. A complex peptide mixture derived from a tryptic digest of porcine liver extract was spiked with α-casein and two synthetic phosphopeptides. The samples were subsequently processed using the ProteoExtract" Phosphopeptide Enrichment Kit TiO_2 Kit. Mass spectrometry analysis was performed using ESI-LC/MS equipment operated in positive mode. (A): unprocessed sample and (B): Phosphopeptides recovered using the ProteoExtract" Phosphopeptide Enrichment Kit TiO_2 Kit.

Cat. No. 539722 **1 kit** **$285**

InnoZyme™ Calpain1/2 Activity Assay Kit

Assay range: 63-1000 ng/ml

A highly sensitive and specific assay for measuring calpain 1 and 2 activity in cell lysates or tissue extracts and for screening enzyme calpain inhibitors. The substrate used in this assay (DQABCYL)-TPLKSPPPSPR-(EDANS) is based on the finding that amino acid preferences for calpain recognition/cleavage extend to 11 positions around the scissile amide bond. Cleavage of the K-S bond relieves internal quenching resulting in increase in fluorescence (*Exc. Max.* 320 nm and *Em. Max. 480 ± 20 nm).*



A: Activity of Calpain 1, Human Erythrocytes (Cat. No. 208713)
B: Activities of Calpain 2, Porcine Kidney (Cat. No. 208715) and Calpain 2, Rat, Recombinant, High Purity, *E. coli* (Cat. No. 208718)

Cat. No. CBA054 **1 kit** **$364**

Transdermal Hormone Delivery Peptide, TD-1

(H-ACSSSPSKHCG-OH, Cyclic)

A highly hydrophilic [Cys-Cys] cyclic 11-mer peptide that facilitates transdermal protein drug delivery by creating a transient opening in the skin barrier. Topical coadministration of TD-1 has been shown to enable insulin and human growth hormone to reach systemic circulation in rats *in vivo*. *Purity: ≥97% by HPLC*. M.W. 1061.2

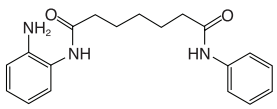
Cat. No. 616365 **5 mg** **$192**

NEW Histone Deacetylase Inhibitors

Histone Deacetylase Inhibitor IV

(N^1-(2-Aminophenyl)-N^7-phenylheptanediamide)

A cell-permeable, specific inhibitor of HDAC. Shown to reverse the silencing of *FXN* transcription in FRDA (Friedreich's ataxia) cells due to hypoacetylation of histones H3 and H4 by increasing acetylation at H3K14, H4K5 and H4K12, without significant changes in acetylation at H3K9, H4K8 and H4K16. *Purity: ≥97% by HPLC*. M.W. 325.4



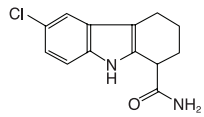
Cat. No. 382170 **10 mg** **$192**

Ref.: Herman, D., et al. 2006. *Nat. Chem. Biol.* **2,** 551.

SIRT1 Inhibitor III

(6-Chloro-2,3,4,9-tetrahydro-1H-carbazole-1-carboxamide, racemic)

A cell-permeable, potent, and highly selective inhibitor of SIRT1 (IC_{50} = 98 nM). Inhibits other sirtuin family deacetylases only at much higher concentrations (IC_{50} = 19.6 and 48.7 µM for SIRT2 and SIRT3, respectively). *Purity: ≥95% by HPLC*. M.W. 248.7



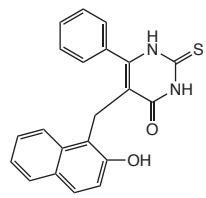
Cat. No. 566322 **5 mg** **$185**

Ref.: Solomon, J.M., et al. 2006. *Mol. Cell. Biol.* **26,** 28; Napper, A.D., et al. 2005. *J. Med. Chem.* **48,** 8045.

SIRT1/2 Inhibitor IV, Cambinol

(NSC-112546)

A cell-permeable inhibitor of NAD-dependent deacetylase activity of hSIRT1 and hSIRT2 (IC_{50} = 56 µM and 59 µM, respectively) in a substrate-, but not NAD-, competitive manner. It inhibits SIRT5 deacetylase activity only at much higher concentrations (IC_{50} > 300 µM). *Purity: ≥95% by HPLC*. M.W. 360.4



Cat. No. 566323 **5 mg** **$145**

Ref.: Heltweg, B., et al. 2006. *Cancer Res.* **66,** 4368.

For more information or to order Calbiochem products, contact EMD

Orders
Phone 800 854 3417
Fax 800 776 0999

Technical Support
Phone 800 628 8470
E-mail calbiochem@emdchemicals.com

Visit our website
www.emdbiosciences.com/calbiochem

You can also order Calbiochem products through our distribution partner, VWR International
Phone 800 932 5000
Web www.vwr.com

Printed in the USA

EMD

P.O. Box 12087
La Jolla, CA 92039-2087

CHANGE SERVICE REQUESTED

PRSRT STD
U.S. POSTAGE
PAID
CITY, STATE
PERMIT NO. #

10001812
Biologics 33.2 2007 USD