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# Biologics

NF- $\kappa$ B Activation: A Link Between  
Chronic Inflammation and Cancer



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# NF- $\kappa$ B Activation: A Link Between Chronic Inflammation and Cancer

Chandra Mohan, Ph.D., EMD Biosciences, Inc.

Inflammation is a normal physiological response to injury or infection, where the inflammatory response isolates the damaged area, mobilizes effector cells and molecules to the site of damage, and ultimately promotes healing. The inflammatory response includes the transcriptional activation of several pro-inflammatory genes, which leads to the release of pro-inflammatory cytokines and chemokines, adhesion molecules, and reactive oxygen and nitrogen species. Simultaneously, anti-inflammatory pathways are also activated that serve as counter-regulatory measures to keep the inflammatory response in check. The inflammatory response can be either acute or chronic. Acute inflammation may last only for a few days and can be easily treated with non-steroidal anti-inflammatory drugs (NSAID). However, chronic inflammation can last for several weeks or months and can cause severe tissue damage.

Inflammation resulting from chronic exposure to infectious and non-infectious agents is an important factor in tumor development. Production and release of free radicals at the site of inflammation can be helpful in eliminating invading pathogens and foreign bodies, but these free radicals can also damage healthy epithelial and stromal cells, which may eventually lead to malignancy. In addition, excessive lipid peroxidation, protein nitration, and DNA damage caused by free radicals can activate pathways that lead to the transcriptional activation of several proto-oncogenes. Furthermore, certain pro-inflammatory cytokines that are encoded by the target genes of nuclear factor  $\kappa$ B (NF- $\kappa$ B) are also linked to tumor development and progression. The inflammatory link to carcinogenesis is also supported by the fact that the NF- $\kappa$ B signal transduction pathway is shown to be dysregulated in a variety of human cancers, especially those of lymphoid cell origin. Several human lymphoid cancer cells are reported to have either mutations or amplifications of genes encoding NF- $\kappa$ B transcription factors.

NF- $\kappa$ B plays an important role in regulating inflammatory and autoimmune responses, cell proliferation, and apoptosis by regulating the expression of genes encoding inflammatory cytokines, cell adhesion molecules, and cyclooxygenase-2 (COX-2). NF- $\kappa$ B is known to be activated by over 450 different activators, including oxidative stress, mitogens, bacteria, and mediators of

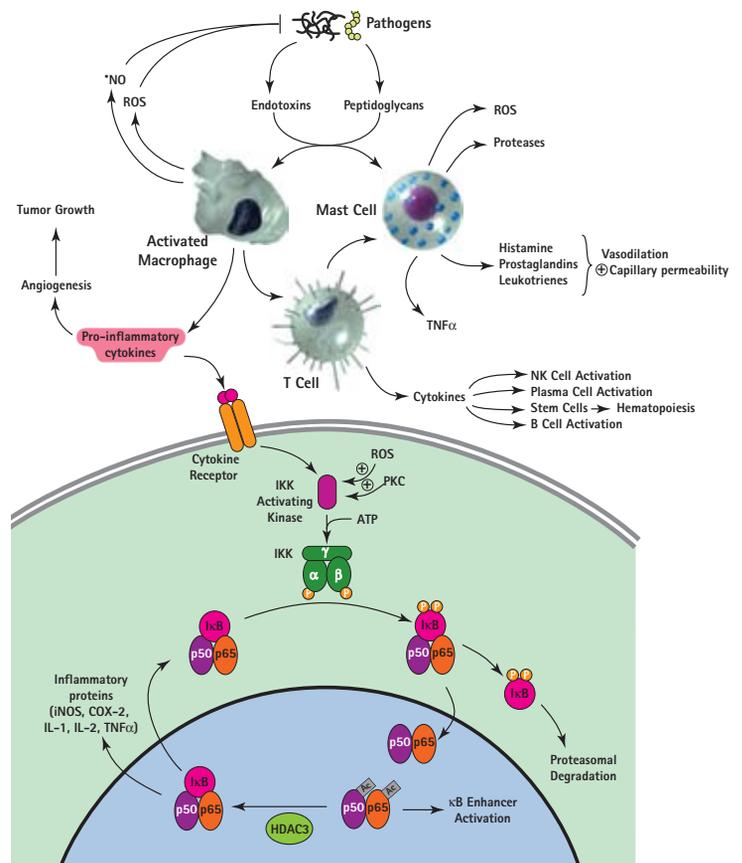
apoptosis. The activation of NF- $\kappa$ B occurs either via the classical pathway, which is triggered by bacterial and viral infections and pro-inflammatory cytokines, or by the alternate pathway, which is activated by members of the Tumor Necrosis Factor (TNF) family. The two pathways switch on different sets of genes and therefore mediate different immune functions. Five members of the NF- $\kappa$ B family have been identified: NF- $\kappa$ B1 (p50/p105), NF- $\kappa$ B2 (p52/p100), RelA (p65), RelB, and c-Rel. They share a highly conserved Rel homology domain (RHD), which is responsible for DNA binding, dimerization, and interaction with I $\kappa$ Bs. The p50/RelA (p65) heterodimer is the major Rel/NF- $\kappa$ B complex in most cells. The activity of NF- $\kappa$ B is tightly regulated by its interaction with inhibitory I $\kappa$ B proteins. In most resting cells, NF- $\kappa$ B is sequestered in the cytoplasm in an inactive form associated with inhibitory molecules such as I $\kappa$ B $\alpha$ , I $\kappa$ B $\beta$ , I $\kappa$ B $\epsilon$ , p105, and p100. This interaction blocks the ability of NF- $\kappa$ B to bind to DNA. Following exposure to pro-inflammatory cytokines, UV light, reactive oxygen species, or bacterial and viral toxins, the NF- $\kappa$ B signaling cascade is activated, leading to the complete degradation of I $\kappa$ B. This allows the translocation of unmasked NF- $\kappa$ B from the cytoplasm to the nucleus where it binds to NF- $\kappa$ B response elements in target genes and regulates their transcription. Among the NF- $\kappa$ B-regulated genes involved in managing the response to inflammation are those encoding for iNOS, COX-2, TNF $\alpha$ , IL-1, IL-6, IL-8, and others. Some of these molecules have also been linked to carcinogenesis. Studies have shown that NF- $\kappa$ B is constitutively active in many types of human tumors.

The activation of NF- $\kappa$ B by extracellular inducers depends on the phosphorylation and subsequent degradation of I $\kappa$ B proteins. Activation of NF- $\kappa$ B is achieved through the action of a family of serine/threonine kinases known as I $\kappa$ B kinase (IKK). IKK contains two catalytic subunits (IKK $\alpha$  and IKK $\beta$ ) and a regulatory/adaptor protein NEMO (also known as IKK $\gamma$ ). IKK activity and NF- $\kappa$ B activation are largely dependent on the integrity of NEMO and IKK $\beta$ . Cells devoid of IKK $\alpha$  can still show normal induction of NF- $\kappa$ B-DNA-binding in response to stimuli. IKK $\alpha$  and IKK $\beta$  phosphorylate I $\kappa$ B proteins and the members of the NF- $\kappa$ B family. All I $\kappa$ B proteins contain two conserved serine residues within their N-terminal region, which are phosphorylated by IKK. IKK $\alpha$  and IKK $\beta$  share about

50% sequence homology and can interchangeably phosphorylate Ser<sup>32/36</sup> of IκBα, and Ser<sup>19/23</sup> of IκBβ. These phosphorylation events lead to the immediate polyubiquitination of IκB proteins and rapid degradation by the 26S proteasome complex.

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, which enhance its DNA binding activity. Several protein kinases, including PKA, PKC, and casein kinase II directly phosphorylate p65 (at Ser<sup>276</sup>, Ser<sup>311</sup>, Ser<sup>529</sup>, respectively). However, others like PI 3-K/Akt and NIK (NF-κB-inducing kinase) phosphorylate IKK, which in turn phosphorylates p65 at Ser<sup>536</sup>. 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<sup>218, 221, 310</sup> for modification. Acetylated NF-κB is active and is resistant to the inhibitory effects of IκB. Deacetylation of p65 by histone deacetylase 3 (HDAC3) promotes its binding to IκB and 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 complex back to the cytoplasm to restore its original latent state.

Unlike normal cells, in most cancer cells NF-κB is constitutively active and resides in the nucleus. In some cases, this is due to chronic stimulation of the IKK pathway, while in others the gene encoding IκBα may be defective. Such constitutive nuclear NF-κB activity not only protects cancer cells from apoptotic cell death, but may also enhance their growth activity. Hence, designing antitumor agents to block NF-κB activity may have great therapeutic value. Researchers have been exploring possibilities of interfering with NF-κB activation and its binding to DNA. They include inhibition of NF-κB dimerization, inhibition of NF-κB activation, use of proteasome inhibitors that block IκB degradation, and inhibition of NF-κB nuclear translocation. Since IKKα and IKKβ are shown to only phosphorylate proteins involved in NF-κB signaling, they are considered as important targets for the development of chemotherapeutic agents.



## References:

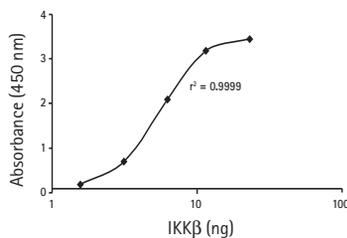
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## NEW Kits for NF- $\kappa$ B Pathway Research

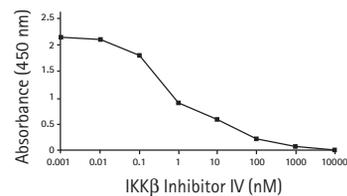
### K-LISA™ IKK $\beta$ Inhibitor Screening Kit

The 96-well K-LISA™ IKK $\beta$ -Inhibitor Screening Kit is designed for rapid *in vitro* screening of IKK $\beta$  inhibitors. The assay is an ELISA-based activity assay that utilizes a 50-amino acid GST-I $\kappa$ B $\alpha$  fusion polypeptide substrate, which includes the Ser<sup>32</sup> and Ser<sup>36</sup> IKK $\beta$  phosphorylation sites. The GST-I $\kappa$ B $\alpha$  substrate and IKK $\beta$  are incubated in the presence of IKK $\beta$  inhibitors in the wells of a glutathione coated 96-well plate, which allows for substrate phosphorylation and capture in a single step. The phosphorylated GST-I $\kappa$ B $\alpha$  substrate is detected using an Anti-Phospho I $\kappa$ B $\alpha$  (Ser<sup>32</sup>/Ser<sup>36</sup>) antibody, followed by an HRP-conjugate and color development with TMB substrate. Assay Range: 5-10 ng.

Cat. No. CBA044      1 kit      € 329



Enzyme activity of purified recombinant IKK $\beta$ . The activity of IKK $\beta$ , His•Tag®, Human Recombinant, *Spodoptera frugiperda* (Cat. No. 481408) was measured as outlined in the user protocol.



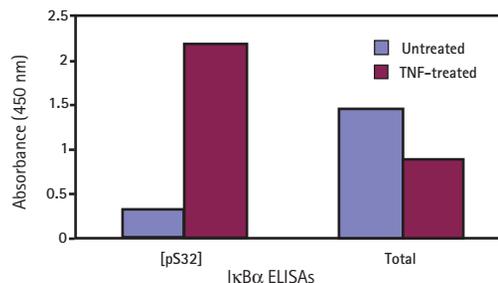
Inhibition of IKK $\beta$  activity by IKK $\beta$  Inhibitor IV (Cat. No. 401481). IKK $\beta$ , His•Tag®, Human Recombinant, *Spodoptera frugiperda* (Cat. No. 481408) (5 ng) was incubated in the presence of increasing concentrations of IKK $\beta$  Inhibitor IV and 10 mM ATP.

### PhosphoDetect™ I $\kappa$ B $\alpha$ (pSer<sup>32</sup>) ELISA Kit

A 96-well solid phase sandwich ELISA that detects and quantifies the level of I $\kappa$ B $\alpha$  phosphorylated at Ser<sup>32</sup> in human cells. Micro strips provided are coated with monoclonal antibody specific for human I $\kappa$ B $\alpha$  (regardless of the phosphorylation state). During the first incubation, the I $\kappa$ B $\alpha$  binds to the immobilized antibody. After washing, an antibody specific for I $\kappa$ B $\alpha$  (pSer<sup>32</sup>) is added to the wells. During the second incubation, this antibody serves as a detection antibody by binding to the immobilized I $\kappa$ B $\alpha$  protein captured during the first incubation. Sensitivity: <5 units/ml of human I $\kappa$ B $\alpha$  (pSer<sup>32</sup>).

Cat. No. CBA065      1 kit      € 518

Detection of phospho- and total I $\kappa$ B $\alpha$  (200  $\mu$ g/ml Jurkat cell lysate)

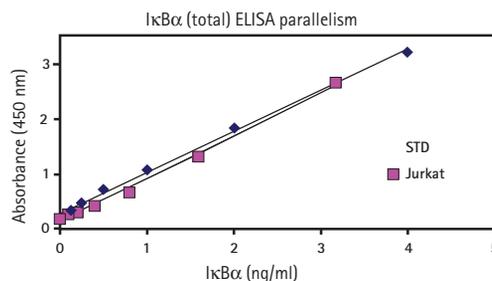


I $\kappa$ B $\alpha$  in TNF- $\alpha$  treated Jurkat cells. TNF- $\alpha$  stimulates the phosphorylation of I $\kappa$ B $\alpha$  at Ser<sup>32</sup> and Ser<sup>36</sup> and marks it for proteasomal degradation. Note that TNF- $\alpha$  treated cells have lower levels of total I $\kappa$ B $\alpha$ .

### I $\kappa$ B $\alpha$ ELISA Kit

A 96-well based solid phase sandwich ELISA that detects and quantifies the level of I $\kappa$ B $\alpha$  independent of its phosphorylation state in human cells. The 96-well plate provided is coated with a monoclonal antibody specific for human I $\kappa$ B $\alpha$ . During the first incubation, the I $\kappa$ B $\alpha$  binds to the immobilized antibody. After washing, an antibody specific for total I $\kappa$ B $\alpha$  is added to the wells. During the second incubation, this antibody serves as a detection antibody by binding to the immobilized I $\kappa$ B $\alpha$  protein captured during the first incubation. Sensitivity: <30 pg/ml.

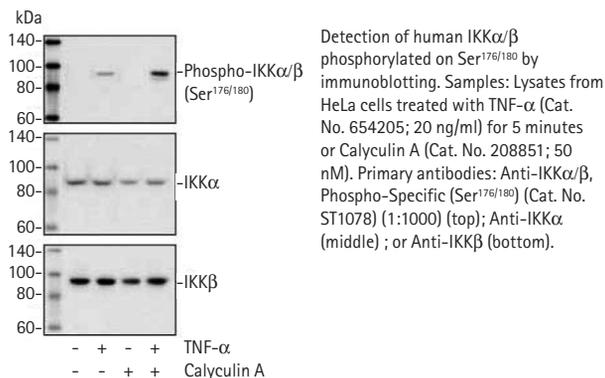
Cat. No. CBA064      1 kit      € 518



Sample: Jurkat cell lysates serially diluted in diluent buffer. Absorbance of each diluted sample was plotted against the I $\kappa$ B $\alpha$  standards.

### PhosphoDetect™ Anti-IKK $\alpha/\beta$ (pSer<sup>176/180</sup>) Rabbit pAb

Liquid, protein A and immunoaffinity purified. Immunogen used was a synthetic peptide corresponding to amino acids surrounding the Ser<sup>176/180</sup> phosphorylation sites of human IKK $\alpha$ . Recognizes the ~85 kDa IKK $\alpha$  protein phosphorylated at Ser<sup>176/180</sup> and the ~87 kDa IKK $\beta$  protein phosphorylated at Ser<sup>177/181</sup>. Reacts with human. IB



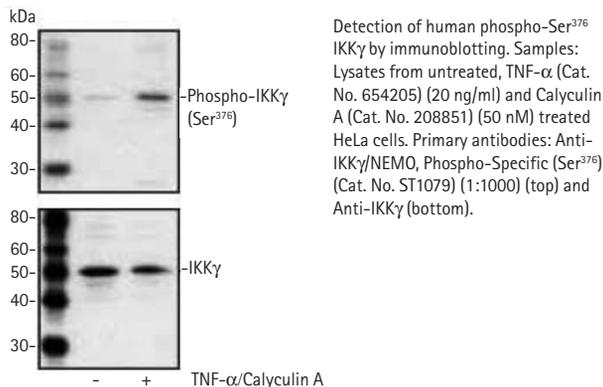
Cat. No. ST1078

50  $\mu$ l

€ 168

### PhosphoDetect™ Anti-IKK $\gamma$ /NEMO (pSer<sup>376</sup>) Rabbit pAb

Liquid, protein A and immunoaffinity purified. Immunogen used was a synthetic peptide corresponding to amino acids surrounding the Ser<sup>376</sup> phosphorylation site of human IKK $\gamma$ . Recognizes the ~50 kDa IKK $\gamma$  protein phosphorylated at Ser<sup>376</sup>. Reacts with human. IB



Cat. No. ST1079

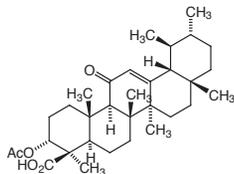
50  $\mu$ l

€ 168

## NF- $\kappa$ B Pathway Activation Inhibitors

### Acetyl-11-keto- $\beta$ -Boswellic Acid, *Boswellia serrata* (3-O-Acetyl-11-keto- $\beta$ -Boswellic Acid; AK $\beta$ BA)

A cell-permeable pentacyclic triterpene of the ursane type that displays antitumor and anti-inflammatory properties. Shown to block the phosphorylation and degradation of I $\kappa$ B $\alpha$  and inhibit NF- $\kappa$ B-mediated gene transcription in chemoresistant, androgen-independent PC-3 prostate cancer cells (~10  $\mu$ M). Purity:  $\geq 98\%$  by HPLC. M.W. 512.7



Cat. No. 110123

5 mg

€ 147

Ref.: Syrovets, T., et al. 2005. *J. Biol. Chem.* 280, 6170; Altmann, A., et al. 2004. *Br. J. Pharmacol.* 141, 223; Altmann, A., et al. 2002. *Biochem. Biophys. Res. Commun.* 290, 185; Hoernlein, R.F., et al. 1999. *J. Pharmacol. Exp. Ther.* 288, 613.

### Evodiamine, *Evodia rutaecarpa*

A cell-permeable quinazolinocarboline alkaloid that suppresses both inducible and constitutive NF- $\kappa$ B activation and NF- $\kappa$ B-regulated gene expression by inhibiting I $\kappa$ B $\alpha$  kinase (IKK) activation. Purity:  $\geq 95\%$  by HPLC. M.W. 303.4

Cat. No. 341211

5 mg

€ 165

Ref.: Takada, Y., et al. 2005. *J. Biol. Chem.* 280, 17203; Liao, C.H., et al. 2005. *Carcinogenesis* 26, 968; Huang, Y.C., et al. 2004. *Life Sci.* 75, 35; Ogasawara, M., and Suzuki, H. 2004. *Biol. Pharm. Bull.* 27, 578; Fei, X.F., et al. 2003. *Cancer Sci.* 94, 92; Chiou, W.F., et al. 1992. *Eur. J. Pharmacol.* 215, 277.

### IKK Inhibitor III, BMS-345541

A cell-permeable, potent, selective, and allosteric site-binding inhibitor of IKK-2 (IC<sub>50</sub> ~300 nM). Exhibits ~10-fold greater selectivity over IKK-1 (IC<sub>50</sub> ~ 4.0  $\mu$ M) and no significant activity towards IKK $\epsilon$  and several other protein kinases. Inhibits cellular I $\kappa$ B $\alpha$  phosphorylation (IC<sub>50</sub> = 4  $\mu$ M in THP-1 cells) and LPS-induced cytokine production both *in vitro* (IC<sub>50</sub> = 1-5  $\mu$ M in THP-1 cells) and *in vivo* (IC<sub>50</sub> = 10 mg/kg in mice). Purity:  $\geq 96\%$  by HPLC. M.W. 255.3

Cat. No. 401480

1 mg

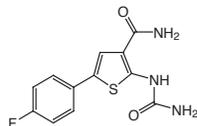
€ 184

## NF-κB Activation Inhibitors (continued...)

### IKK-2 Inhibitor IV

{[5-(*p*-Fluorophenyl)-2-ureido]thiophene-3-carboxamide}

A cell-permeable, potent, and selective inhibitor of IKK-2 ( $IC_{50}$  = 18 nM) with selectivity over IKK-1, JNK, and p38 MAPK. *Purity*: ≥95% by HPLC. M.W. 279.3



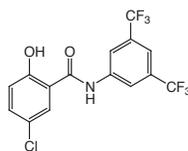
Cat. No. 401481      500 μg      € 98

Ref.: Podolin, P.L., et al. 2005. *J. Pharmacol. Exp. Ther.* 312, 373; Karin, M., et al. 2004. *Nat. Rev. Drug Discov.* 3, 17; Roshak, A.K., et al. 2002. *Inflamm. Res.* 51, 54.

### IKK-2 Inhibitor V

[N-(3,5-Bis-trifluoromethylphenyl)-5-chloro-2-hydroxybenzamide; IMD-0354]

An IKK-2 inhibitor that selectively blocks IκBα phosphorylation ( $IC_{50}$  ~ 250 nM). *Purity*: ≥95% by HPLC. M.W. 383.7



Cat. No. 401482      5 mg      € 189

Ref.: Kamon, J., et al. 2004. *Biochem. Biophys. Res. Commun.* 323, 242; Onai, Y., et al. 2004. *Cardiovasc. Res.* 63, 51; Tanaka, A., et al. 2004. *Blood* 105, 2324.

### InSolution™ IKK-2 Inhibitor, SC-514

A 25 mM (1 mg/178 μl) solution of IKK-2 Inhibitor, SC-514 (Cat. No. 401479) in DMSO. A cell-permeable, potent, reversible, ATP-competitive, and highly selective inhibitor of IKK-2 ( $IC_{50}$  ~3-12 μM for IKK-2 homodimer, IKK-1/IKK-2 heterodimer, and IKK-2). *Purity*: ≥95% by HPLC. M.W. 224.3

Cat. No. 401485      1 mg      € 69

Ref.: Baxter, A., et al. 2004 *Bioorg. Med. Chem. Lett.* 14, 2817; Kishore, N., et al. 2003. *J. Biol. Chem.* 278, 32861.

### IKKβ, His•Tag® and S•Tag™, Human Recombinant, *Spodoptera frugiperda*

A full-length, recombinant, human IKKβ (amino acids 1-756) expressed in *Spodoptera frugiperda* insect cells with N-terminal His•Tag® and S•Tag™ sequences.

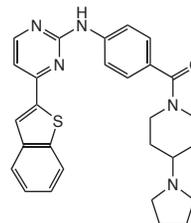
*Specific activity*: ≥50 units/mg protein. *Purity*: ≥80% by SDS-PAGE

Cat. No. 481404      10 μg      € 270

Ref.: Greten, F.R., et al. 2004. *Cell* 118, 285; Baldwin, A.S. 2001. *J. Clin. Invest.* 107, 241; Yamamoto, Y. and Gaynor, R.B. 2001. *J. Clin. Invest.* 107, 135; Karin, M., et al. 2000. *Annu. Rev. Immunol.* 18, 621; Zandi, E., et al. 1997. *Cell* 91, 243.

### IKK Inhibitor VII

A cell-permeable, potent, selective, and ATP-competitive inhibitor of IKK ( $IC_{50}$  = 40 nM, 70 nM, and 200 nM for IKK-2, IKK complex, and IKK-1, respectively). Inhibits cellular IκBα degradation and NF-κB-mediated gene expression *in vitro* in HUVEC cells. *Purity*: ≥97% by HPLC. M.W. 483.6



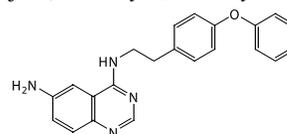
Cat. No. 401486      1 mg      € 104

Ref.: Waelchli, R., et al. 2006. *Bioorg. Med. Chem. Lett.* 16, 108.

### NF-κB Activation Inhibitor

[6-Amino-4-(4-phenoxyphenylethylamino)quinazoline]

A cell-permeable, potent inhibitor of NF-κB transcriptional activation ( $IC_{50}$  = 11 nM in Jurkat cells) and LPS-induced TNF-α production ( $IC_{50}$  = 7 nM in murine splenocytes). *Purity*: ≥98% by HPLC. M.W. 356.4



Cat. No. 481406      1 mg      € 94

Ref.: Tobe, M., et al. 2003. *Bioorg. Med. Chem.* 11, 383.

### InSolution™ NF-κB Activation Inhibitor

A 10 mM (1 mg/281 μl) solution of NF-κB Activation Inhibitor (Cat. No. 481406) in DMSO. *Purity*: ≥98% by HPLC. M.W. 356.4

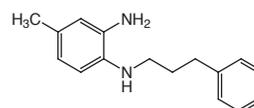
Cat. No. 481407      1 mg      € 69

Ref.: Tobe, M., et al. 2003. *Bioorg. Med. Chem.* 11, 383.

### NF-κB Activation Inhibitor II, JSH-23

[4-Methyl-N'-(3-phenylpropyl)benzene-1,2-diamine]

A cell-permeable, selective blocker of nuclear translocation of NF-κB p65 and its transcription activity ( $IC_{50}$  = 7.1 μM in a NF-κB reporter assay using RAW 264.7 cells) without affecting IκB degradation. *Purity*: ≥95% by HPLC. M.W. 240.3



Cat. No. 481408      5 mg      € 104

Ref.: Shin, H.M., et al. 2004. *FEBS Lett.* 571, 50.

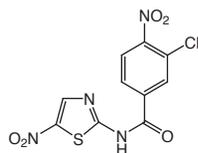
## NF- $\kappa$ B Activation Inhibitors (continued...)

### NF- $\kappa$ B Activation Inhibitor III

[3-Chloro-4-nitro-N-(5-nitro-2-thiazolyl)-benzamide; SM-7368]

A cell-permeable inhibitor of TNF- $\alpha$ -stimulated NF- $\kappa$ B activation and subsequent upregulation of MMP-9 in HT1080 cells (complete inhibition at 10  $\mu$ M). Does not affect TNF- $\alpha$ -induced AP-1 activity. The cellular target appears to be downstream of p38 activation.

Purity:  $\geq 98\%$  by HPLC. M.W. 328.7



Cat. No. 481411      5 mg      € 99

Ref.: Lee, H.Y., et al. 2005. *Biochem. Biophys. Res. Commun.* 336, 716.

### NF- $\kappa$ B SN50, Cell-Permeable Inhibitor Peptide (AAVALLPAVLLALLAPVQRKRQKLMP)

Contains the nuclear localization sequence (NLS) of the transcription factor NF- $\kappa$ B p50 linked to the hydrophobic region (h-region) of the signal peptide of Kaposi fibroblast growth factor (K-FGF). The peptide N-terminal K-FGF h-region confers cell-permeability, while the NLS (360-369) inhibits translocation of the NF- $\kappa$ B active complex into the nucleus. Purity:  $\geq 97\%$  by HPLC. M.W. 2781.5

Cat. No. 481480      500  $\mu$ g      € 185

Ref.: Lin, Y.-Z., et al. 1995. *J. Biol. Chem.* 270, 14255.

### Oridonin, *R. rubescens*

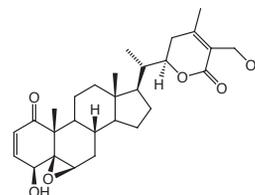
A cell-permeable diterpenoid compound that possesses anti NF- $\kappa$ B activity. Shown to efficiently block both LPS-induced NF- $\kappa$ B activity in Jurkat and in RAW 264.7 murine macrophages, and inhibit NF- $\kappa$ B transcriptional activity (IC<sub>50</sub>  $\sim$  5  $\mu$ g/ml in MT-1 cells) by disrupting NF- $\kappa$ B DNA-binding activity without interfering with its nuclear translocation. Purity:  $\geq 95\%$  by HPLC. M.W. 364.4

Cat. No. 496915      5 mg      € 72

Ref.: Ikezoe, T., et al. 2005. *Mol. Cancer Ther.* 4, 578; Meade-Tollin, L.C., et al. 2004. *J. Nat. Prod.* 67, 2.

### Withaferin A, *Withania somnifera*

A cell-permeable steroidal lactone that displays antitumor, anti-inflammatory, radiosensitizing, and immunosuppressive properties. Potently inhibits angiogenesis (IC<sub>50</sub> = 12 nM for HUVEC proliferation and 7  $\mu$ g/kg/day in C57BL/6J mice, i.p.) and blocks NF- $\kappa$ B activation (IC<sub>50</sub> = 500 nM in TNF- $\alpha$ -induced endothelial cells) by targeting the ubiquitin-mediated proteasome pathway. Purity:  $\geq 95\%$  by HPLC. M.W. 470.6



Cat. No. 681535      1 mg      € 88  
5 mg      € 300

Ref.: Mohan, R., et al. 2004. *Angiogenesis* 7, 115; Jeyaprasadam, B., et al. 2003. *Life Sci.* 74, 125; Devi, P.U., et al. 1995. *Cancer Lett.* 95, 189; Kupchan, S.M., et al. 1969. *J. Org. Chem.* 34, 3858.

## PAR-2 Agonists

### PAR-2 Agonist I

(2f-LIGRL-amide; Proteinase Activated Receptor-2 Agonist I)

The native PAR-2-specific agonist, SLIGRL-NH<sub>2</sub>, is modified with an N-terminal fuoyl group to increase its potency and resistance to metabolic degradation. Shown to activate [Ca<sup>2+</sup>]<sub>i</sub> mobilization in PAR-2-expressing cells (EC<sub>50</sub> = 253 nM using HCT-15 cells) *in vitro* and induce PAR-2 mediated salivation (ED<sub>50</sub> = 30 nmol/kg, i.v.) *in vivo*, while exhibiting no effect on PAR-2<sup>-/-</sup> mice. Reactive towards human, rat, and murine PAR-2.

Purity:  $\geq 95\%$  by HPLC. M.W. 663.8

Cat. No. 539109      1 mg      € 92  
5 mg      € 263

Ref.: Kawabata, A., et al. 2004. *J. Pharmacol. Exp. Ther.* 309, 108; Kawabata, A., et al. 2004. *J. Pharmacol. Exp. Ther.* 309, 1098; Ferrell, W.R., et al. 2003. *J. Clin. Invest.* 111, 35.

### PAR-2 Agonist II

(2f-LIGRLO-amide; Proteinase Activated Receptor-2 Agonist II)

A hexapeptide similar to PAR-2 Agonist I (Cat. No. 539109), but with an additional C-terminal ornithine. Increases [Ca<sup>2+</sup>]<sub>i</sub> mobilization in PAR-2-expressing cells (EC<sub>50</sub> = 100 nM using KNRK). Reactive towards human, rat, and murine PAR-2. Purity:  $\geq 98\%$  by HPLC. M.W. 778

Cat. No. 539110      1 mg      € 92  
5 mg      € 263

Ref.: McGuire, J.J., et al. 2004. *J. Pharmacol. Exp. Ther.* 309, 1124.

# Antibodies for MAP Kinase Signaling Research

Name	Cat. No.	Comments	Size	Price
Anti-MAP Kinase ERK1/ERK2 (333-367) Rabbit pAb	442675	Liquid, immunoaffinity purified. Immunogen used was a synthetic peptide corresponding to amino acids 333-367 of rat ERK1 MAP kinase with the CCG spacer group added and the peptide conjugated to KLH. Recognizes the ~42-44 kDa ERK1 and ERK2 proteins. Reacts with most species studied. <b>IB, IH, IP</b>	100 µg	€ 324
PhosphoDetect™ Anti-MAP Kinase ERK1/ERK2 (pThr <sup>202</sup> /Tyr <sup>204</sup> ) Mouse mAb (12D4)	442706	Lyophilized, purified by thiophilic absorption and size exclusion chromatography. Immunogen used was a synthetic phosphopeptide corresponding to amino acids surrounding the pThr-Glu-pTyr sequence motif of mouse ERK1 and ERK2. Recognizes the ~42-44 kDa ERK1 and ERK2 proteins phosphorylated at Thr <sup>202</sup> and Tyr <sup>204</sup> . Reacts with human, mouse, and rat. <b>ELISA, IB, IP</b>	1 set	€ 328
PhosphoDetect™ Anti-MAP Kinase ERK1/ERK2 (pThr <sup>202</sup> /Tyr <sup>204</sup> ) Rabbit pAb	442685	Liquid, immunoaffinity purified. Immunogen used was a synthetic phosphopeptide surrounding the Thr <sup>202</sup> /Tyr <sup>204</sup> phosphorylation site of human ERK1/ERK2. Recognizes the ~42-44 kDa ERK1 and ERK2 proteins phosphorylated at Thr <sup>202</sup> and Tyr <sup>204</sup> . Reacts with human and rat. <b>DB, IB</b>	100 µl	€ 320
Anti-MAP Kinase ERK1/ERK2 Rabbit pAb	442704	Liquid, protein A purified. Immunogen used was a synthetic peptide corresponding to amino acids from rat p42 MAP kinase conjugated to KLH. Recognizes the ~42-44 kDa ERK1 and ERK2 proteins. Reacts with hamster, human, mouse, rat, and zebrafish. <b>FC, IB, PS</b>	200 µl	€ 329
Anti-MAP Kinase ERK2, N-Terminal (6-17) Rabbit pAb	442680	Liquid, immunoaffinity purified. Immunogen used was a synthetic peptide corresponding to amino acids 6-17 of rat ERK2, with a cysteine (C) added and the peptide conjugated to KLH. Recognizes the ~42 kDa ERK2 protein in various human, mouse, and rat tissues. Also reacts with <i>Xenopus</i> ovary tissue extracts. <b>IB</b>	100 µg	€ 324

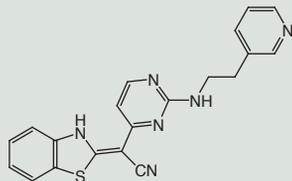
**DB:** Dot blot; **ELISA:** enzyme-linked immunosorbent assay; **FC:** flow cytometry; **IB:** immunoblotting; **IH:** immunohistochemistry; **IP:** immunoprecipitation

## **NEW** MAP Kinase Inhibitors

Name	Cat. No.	Comments	Size	Price
ERK Activation Inhibitor Peptide I, Cell-Permeable	328000	A stearated 13-amino acid peptide corresponding to the N-terminus of MEK1. Acts as a specific inhibitor of ERK activation and the transcriptional activity of Elk1. Selectively binds to ERK2 and prevents its interaction with MEK ( $IC_{50} = 2.5 \mu M$ ). <i>Purity: ≥95% by HPLC.</i>	1 mg	€ 156
ERK Activation Inhibitor Peptide II, Cell-Permeable	328005	A 13-amino acid peptide corresponding to the N-terminus of MEK1 that is fused to the HIV-TAT membrane translocating peptide (MTP) sequence via a glycine linker. Acts as a specific inhibitor of ERK activation and the transcriptional activity of Elk1 by binding to ERK2, and prevents its interaction with MEK ( $IC_{50} = 210 nM$ ). <i>Purity: ≥95% by HPLC.</i>	1 mg	€ 208
ERK Inhibitor II	328007	A cell-permeable, potent, ATP-competitive inhibitor of ERK1 and ERK2 ( $IC_{50} = 510 nM$ and $330 nM$ , respectively). Exhibits ~20-fold greater selectivity over p38α ( $IC_{50} = 10 \mu M$ ) and ~60-fold greater selectivity over IKKα, MEK1, MKK4, PDGFRα, PKCα, Src and Syk ( $IC_{50} > 30 \mu M$ ). <i>Purity: ≥98% by HPLC.</i>	1 mg	€ 122
ERK Inhibitor II, Negative Control	328008	A cell-permeable negative control for ERK Inhibitor II (Cat. No. 328007). Shown to poorly inhibit ERK1 and ERK2 ( $IC_{50} > 100 \mu M$ ). <i>Purity: ≥98% by HPLC.</i>	1 mg	€ 122
ERK Inhibitor	328006	A cell-permeable anti-proliferative agent that preferentially binds to ERK2 with a $K_d$ of ~5 µM and prevents its interaction with protein substrates. Blocks ERK-mediated phosphorylation of ribosomal S6 kinase-1 and Elk-1 in HeLa cells. Does not significantly affect ERK1/2 phosphorylation by MEK1/2. <i>Purity: ≥95% by HPLC.</i>	5 mg	€ 77

### JNK Inhibitor V

A cell-permeable, potent, and ATP-competitive inhibitor of c-Jun N-terminal kinase (JNK,  $IC_{50} = 150, 220, \text{ and } 70 nM$  for hJNK1, hJNK2, and hJNK3, respectively) with a 10- to 100-fold greater selectivity over a panel of 25 other commonly studied kinases. *Purity: ≥95% by HPLC (sum of two isomers).*



Cat. No. 420129      5 mg      € 126



## **NEW** Recombinant MAP Kinases

### MAP Kinase 1, His•Tag®, Activated, Human, Recombinant, *E. coli*

Purified recombinant human MAP Kinase 1 (ERK1) expressed in *E. coli*. Highly active form produced by phosphorylation of the purified MAP Kinase *in vitro* with MEK1. Suitable for labeling MAP kinase substrates. Features a His•Tag® sequence to facilitate the removal of MAP kinase from the reaction mixture. *Specific activity*:  $\geq 6000$  units/mg protein. *Purity*:  $\geq 95\%$  by SDS-PAGE

Cat. No. 454849      2.5 µg      € 325

Ref.: Charest, D.L., et al. 1993. *Mol. Cell Biol.* 13, 4679.

### MAP Kinase 2, His•Tag®, Activated, Rat, Recombinant, *E. coli*

Purified recombinant rat skeletal muscle MAP kinase (ERK2) expressed in *E. coli*. Highly active form of MAP kinase that is produced by phosphorylating non-activated MAP Kinase (Cat. No. 454852) *in vitro* with a constitutively active MEK mutant. Suitable for labeling MAP kinase substrates. Features a His•Tag® sequence to facilitate removal of MAP kinase from the reaction mixture. *Specific activity*:  $\geq 600,000$  units/mg protein. *Purity*:  $\geq 95\%$  by SDS-PAGE

Cat. No. 454855      5 µg      € 402

Ref.: Zheng, C.-F., and Guan, K.L. 1994. *EMBO J.* 13, 1123; Robbins, D.J., et al. 1993. *J. Biol. Chem.* 268, 5097; Boulton, T.G., et al. 1991. *Cell* 65, 663.

### MAP Kinase 2, Activated, Mouse, Recombinant, *E. coli*

Coexpressed with MEK, phosphorylated and active. *Purity*:  $\geq 90\%$  by SDS-PAGE

Cat. No. 454850      2000 U      € 306

Ref.: Fukunaga, K., and Miyamoto, E. 1998. *Mol. Neurobiol.* 16, 79; Wu, J., et al. 1993. *Mol. Cell Biol.* 13, 4539.

### [Ala<sup>71</sup>]-MAP Kinase ERK1, Inactive, Human, Recombinant, Agarose Conjugate

ERK1 with Lys<sup>71</sup> to Ala<sup>71</sup> mutation that results in a catalytically inactive form of the MAP kinase that can neither autophosphorylate nor phosphorylate other proteins. Suitable for use as a substrate for the detection and quantitation of MEK1 and MEK2.

Cat. No. 442674      100 µg      € 416

Ref.: Pelech, S.L., and Charest, D.L. 1995. *Prog. Cell Cycle Res.* 1, 33; Charest, D.L., et al. 1993. *Mol. Cell Biol.* 13, 4679; Alessandrini, A., et al. 1992. *Proc. Natl. Acad. Sci. USA* 89, 8200.

### MAP Kinase 2, His•Tag®, Non-Activated, Rat, Recombinant, *E. coli*

Purified recombinant rat skeletal muscle MAP kinase (ERK2) expressed in *E. coli*. Suitable to assay activity of MAP kinase activators such as MEK in cell lysates or in chromatography fractions. Features a His•Tag® sequence to facilitate removal of MAP kinase from the reaction mixture. *Specific activity*:  $\geq 1000$  units/mg protein. *Purity*:  $\geq 95\%$  by SDS-PAGE

Cat. No. 454852      20 µg      € 402

Ref.: Zheng, C.-F., and Guan, K.L. 1994. *EMBO J.* 13, 1123; Robbins, D.J., et al. 1993. *J. Biol. Chem.* 268, 5097; Cobb, M.H., et al. 1991. *Cell Regul.* 2, 965.

### MAP Kinase 2, His•Tag®, Activated, Human, Recombinant, *E. coli* (ERK2; MAPK2; p42<sup>MAPK</sup>)

Purified recombinant human MAP Kinase (ERK2) expressed in *E. coli*. Highly active form produced by phosphorylation of the purified MAP Kinase *in vitro* with MEK1. Suitable for labeling MAP Kinase substrates. Features a His•Tag® sequence to facilitate the removal of MAP kinase from the reaction mixture. *Specific activity*:  $\geq 5500$  units/mg protein. *Purity*:  $\geq 95\%$  by SDS-PAGE

Cat. No. 454854      5 µg      € 325

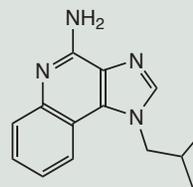
Ref.: Lew, J. 2003. *Biochemistry* 42, 849; Johnson, G.L., and Lapadat, R. 2002. *Science* 298, 1911; Koistinaho, M., and Koistinaho, J. 2002. *Glia* 40, 175.

## **NEW** Toll-Like Receptor-7 Agonist

### Imiquimod

A potent immunomodulator with anti-angiogenic, anti-viral, and anti-inflammatory properties. Binds to the cell surface toll-like receptor 7 (TLR-7) and induces the secretion of several pro-inflammatory cytokines and chemokines both *in vitro* and *in vivo*.

*Purity*:  $\geq 98\%$  by HPLC.M.W. 240.3



Cat. No. 401020      250 mg      € 113

 Visit our Interactive Pathways™: [www.calbiochem.com/MAPK](http://www.calbiochem.com/MAPK)

# Human Recombinant Cytokines for Inflammation Research

Name	Cat. No.	Comments	Size	Price
γ-Interferon, Human, Recombinant, <i>E. coli</i>	407306	Biological activity: ED <sub>50</sub> = 0.5–3.0 ng/ml as measured by inhibition (cytostasis) of human WiDr cells. <i>Purity: ≥95% by SDS-PAGE.</i>	100 µg	€ 547
Interleukin-1α, Human, Recombinant, <i>E. coli</i>	407611	Biological activity: ED <sub>50</sub> = 3–10 pg/ml as measured in a cell proliferation assay. <i>Purity: ≥97% by SDS-PAGE.</i>	2 µg	€ 264
Interleukin-1β, Human, Recombinant, <i>E. coli</i>	407615	Biological activity: ED <sub>50</sub> = 5–10 pg/ml as measured in a cell proliferation assay using the murine helper T-cell line, D10.G4.1. <i>Purity: ≥97% by SDS-PAGE.</i>	5 µg	€ 345
Interleukin-4, Human, Recombinant, <i>E. coli</i>	407635	Biological activity: ED <sub>50</sub> = 50–200 pg/ml as measured in a TF-1 proliferation assay with PHA-activated human peripheral blood lymphocytes. <i>Purity: ≥98% by SDS-PAGE.</i>	5 µg	€ 227
Interleukin-6, Human, Recombinant, <i>E. coli</i>	407652	Biological activity: 8–20 pg/ml as measured in a cell proliferation assay with a factor-dependent murine plasmacytoma cell line, B9. <i>Purity: ≥95% by SDS-PAGE.</i>	10 µg	€ 318
Interleukin-8, Human, Recombinant, <i>E. coli</i>	407673	Biological activity: ED <sub>50</sub> = 150–300 ng/ml as measured by induction of myeloperoxidase release from human neutrophils. <i>Purity: ≥97% by SDS-PAGE.</i>	10 µg	€ 175
Interleukin-10, Human, Recombinant, <i>Spodoptera frugiperda</i>	407700	Biological activity: ED <sub>50</sub> = 0.2–1.0 ng/ml as measured in a cell proliferation assay using a mouse mast cell line, MC/9. <i>Purity: ≥95% by SDS-PAGE.</i>	5 µg	€ 323
Interleukin-12, Human, Recombinant, <i>Spodoptera frugiperda</i>	407711	Biological activity: ED <sub>50</sub> = 50–200 pg/ml as measured by its ability to stimulate the proliferation of PHA-activated human lymphoblasts. <i>Purity: ≥95% by SDS-PAGE.</i>	5 µg	€ 334
Interleukin-13, Human, Recombinant, <i>E. coli</i>	407715	Biological activity: ED <sub>50</sub> = 3.0–6.0 ng/ml as measured in a cell proliferation assay using a human factor-dependent cell line, TF-1. <i>Purity: &gt;97% by SDS-PAGE.</i>	5 µg	€ 348
Macrophage Inflammatory Protein-1α, Human, Recombinant, <i>E. coli</i>	441523	Biological activity: ED <sub>50</sub> = 2.0–10.0 ng/ml as measured by its ability to inhibit mouse hematopoietic stem cell proliferation in an <i>in vitro</i> colony assay that detects primitive cells. <i>Purity: ≥97% by SDS-PAGE.</i>	10 µg	€ 306
Macrophage Inflammatory Protein-1β, Human, Recombinant, <i>Spodoptera frugiperda</i>	441529	Biological activity: ED <sub>50</sub> = 40–60 ng/ml as measured by its ability to inhibit mouse hematopoietic stem cell proliferation in an <i>in vitro</i> colony assay that detects primitive cells. <i>Purity: ≥97% by SDS-PAGE.</i>	10 µg	€ 294
Monocyte Chemoattractant Protein-1, Human, Recombinant, <i>E. coli</i>	475901	Biological activity: ED <sub>50</sub> = 5–20 ng/ml as measured by its monocyte chemotactic activity. <i>Purity: ≥97% by SDS-PAGE.</i>	10 µg	€ 249
Oncostatin M, Human, Recombinant, <i>E. coli</i>	496260	Biological activity: ED <sub>50</sub> = 0.15–0.30 ng/ml as measured in a cell proliferation assay using a factor-dependent human erythroleukemic cell line, TF-1. <i>Purity: ≥97% by SDS-PAGE.</i>	10 µg	€ 352
RANTES, Human, Recombinant, <i>E. coli</i>	553500	Biological activity: ED <sub>50</sub> = 5–20 ng/ml as determined by the dose-dependent chemotaxis of THP-1 cells. <i>Purity: ≥95% by SDS-PAGE.</i>	10 µg	€ 246
Tumor Necrosis Factor-α, Human, Recombinant, <i>E. coli</i>	654205	Biological activity: ED <sub>50</sub> = 20–50 pg/ml as measured in a cytotoxicity assay with the TNF-α-susceptible murine L-929 cell line in the presence of Actinomycin D (Cat. No. 114666). <i>Purity: ≥95% by SDS-PAGE.</i>	10 µg	€ 301

## DNA Damage and Repair Research Tools

### DNA Base Excision Repair Pathway Inhibitor (CRT0044876; 7-Nitroindole-2-carboxylic acid)

A cell-permeable nitroindole carboxylate that acts as a potent, specific, and nontoxic inhibitor of the DNA repair enzyme, APE1 (human apurinic/apyrimidinic endonuclease; IC<sub>50</sub> ~ 3 µM). Shown to target the APE1 active site and inhibit its 3'-phosphodiesterase and 3'-phosphatase activities. Exhibits minimal effects on endonuclease IV, BamH1 restriction endonuclease, or topoisomerase I at 100 µM. Also shown to potentiate the cytotoxicity of several DNA damaging agents, such as MMS, temozolomide, zeocin, and H<sub>2</sub>O<sub>2</sub> in HeLa, HT1080, and MDA-MB-231 cells. *Purity: ≥95% by titration.*

M.W. 206.2

**Cat. No. 262015      25 mg      € 68**

Ref.: Madhusudan, S., et al. 2005. *Nucleic Acids Res.* 33, 4711.

### Flap Endonuclease 1, Human, Recombinant, *S. frugiperda*

(FEN-1, Human, Recombinant, *S. frugiperda*)

A nuclear enzyme involved in DNA replication, repair, recombination, and maintenance of genomic integrity. In all eukaryotes it cleaves the 5' flaps that arise between Okazaki fragments. Also in eukaryotes, FEN-1 repairs defects in DNA. Mutations in the FEN-1 gene cause increased accumulation of mutations and genomic rearrangements. Also promotes DNA fragmentation resulting in apoptosis. *Purity: ≥98% by SDS-PAGE.*

**Cat. No. 662081      100 U      € 383**

Ref.: Solovjeva, L., et al. 2005. *Mol. Cell. Biol.* 16, 2518; Zheng, L., et al. 2005. *EMBO Rep.* 6, 83; Watanabe, K., et al. 2004. *EMBO J.* 23, 3886; Henneke, G., et al. 2003. *Oncogene* 22, 4301; Parrish, J., et al. 2003. *EMBO J.* 22, 3451; Tom, S., et al. 2000. *J. Biol. Chem.* 275, 10498; Warbrick, E., et al. 1997. *Oncogene* 14, 2313; Chen, U., et al. 1996. *Proc. Natl. Acad. Sci. U.S.A.* 93, 11597; Harrington, J.J. and Lieber, M.R. 1994. *EMBO J.* 13, 1235.

# Cyclooxygenase-2 Inhibitors: Their Emerging Role in Cancer and Alzheimer's Disease

Cyclooxygenase (COX) 1 and 2 are bifunctional hemoproteins that catalyze both the bioxygenation of arachidonic acid to form prostaglandin G<sub>2</sub> (PGG<sub>2</sub>) and the peroxidative reduction of PGG<sub>2</sub> to form prostaglandin H<sub>2</sub> (PGH<sub>2</sub>). Hence, COX has two different active sites. On one side, it has the cyclooxygenase active site and on the opposite side, it has an entirely separate peroxidase site, which is required to activate the heme groups that participate in the cyclooxygenase reaction. The enzyme complex is a dimer of identical subunits, two cyclooxygenase active sites and two peroxidase active sites. The active site of COX-2 is slightly larger and can accommodate bigger structures than those that are able to reach the active site of COX-1. COX-1 is a constitutive enzyme associated with the endoplasmic reticulum. It is responsible for maintaining normal physiologic function and is considered as a “housekeeping” enzyme. COX-2 is an inducible enzyme that is mainly associated with the nuclear envelope and is primarily associated with inflammation. Cytokines and growth factors increase the expression of COX-2, mainly at inflammatory sites, producing prostaglandins, which mediate inflammation, pain, and fever. Increased expression of COX-2 has also been associated with increased incidence of colon and breast cancers. COX-2 is shown to be over-expressed in about 50% of adenomas and 85% of adenocarcinomas of the colon. Hence, COX-2 inhibitors offer greater therapeutic promise not only in the treatment of inflammation, but also some forms of cancer. COX-2 inhibitors are also shown to enhance photosensitization by increasing apoptosis and improve photodynamic therapy responsiveness by decreasing expression of angiogenic and inflammatory molecules.

There has been an upsurge of interest in COX-2 inhibitors as possible candidates for the treatment of Alzheimer's disease. This is due to the fact that researchers have begun to think about “inflammation as a factor” in the development and/or progression of Alzheimer's disease. Since neuronal excitation and oxidative stress have been linked to the pathogenesis of several neurodegenerative disorders, inhibiting excessive COX-2 activity may reduce the oxidative stress-induced neuronal damage and trauma.

References: Ho, L., et al. 2006. *CNS Drugs* 20, 85; Mazhar, D., et al. 2006. *Br. J. Cancer* 94, 346; Ferrario, A., et al. 2005. *Cancer Res.* 65, 9473; Hawkey, C.J., and Fortun, P.J. 2005. *Curr. Opin. Gastroenterol.* 21, 660; Patrignani, P., et al. 2005. *Brain Res. Brain Res. Rev.* 48, 352.

## COX-2 ELISA Kit

A 96-well ELISA for detection and quantification of human COX-2 in cell lysates, tissue extracts, and biological fluids. The 96-well plate is coated with a rabbit anti-human COX-2 polyclonal antibody that serves as a capture antibody. Standards and samples are added to the wells that bind to the coated antibody. COX-2 is then detected with a monoclonal anti-COX-2 antibody and a goat anti-mouse IgG HRP conjugate. Assay Range: 2.5-200 ng/ml

Cat. No. CBA053                      1 kit                      € 473



LPS-induced COX-2 expression in U937 cells. Cox-2 was measured using 50 µg total protein as outlined in the user protocol.

## Cyclooxygenase Inhibitor Set

Provided as a 4 vial set. Each set contains 100 mg of Meloxicam (Cat. No. 444800), and 5 mg each of NS-398 (Cat. No. 349254), SC-560 (Cat. No. 565610), and Sulindac Sulfide (Cat. No. 574102).

Cat. No. 239783                      1 set                      € 355

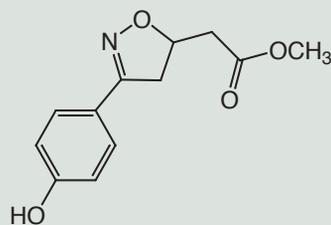
## Selected COX-2 Inhibitors for Inflammation Research

Name	Cat. No.	Comments	Size	Price
COX-2 Inhibitor I	236011	A potent and selective inhibitor of COX-2 ( $IC_{50}$ = 650 nM) from human monocytes. Displays only very weak activity against COX-1 from human platelets ( $IC_{50}$ >10 $\mu$ M) and in whole blood ( $IC_{50}$ >100 $\mu$ M). <i>Purity:</i> $\geq$ 97% by HPLC. M.W. 377.8	5 mg	€ 176
COX-2 Inhibitor II	236012	A cell-permeable isoxazolyl-benzenesulfonamide compound that acts as a potent and highly selective inhibitor of COX-2 both <i>in vitro</i> ( $IC_{50}$ = 4 nM for hCOX-2 vs. 114 $\mu$ M for hCOX-1) and <i>in vivo</i> . <i>Purity:</i> $\geq$ 98% by HPLC. M.W. 350.3	5 mg	€ 118
Diclofenac Sodium	287840	Strongly inhibits insoluble transthyretin (TTR) amyloid fibril formation. A potent inhibitor of COX-1 ( $IC_{50}$ = 76 nM) and COX-2 ( $IC_{50}$ = 26 nM). <i>Purity:</i> $\geq$ 98% by TLC. M.W. 318.1	1 g	€ 32
Diclofenac, 4'-Hydroxy-	287845	A metabolite of Diclofenac (Cat. No. 287840). Formed through oxidation of diclofenac by cytochrome P450 2C9. Suppresses prostaglandin E2 (PGE2) formation by specifically blocking COX-2 activity ( $IC_{50}$ = 16.9 nM). <i>Purity:</i> $\geq$ 97% by HPLC. M.W. 312.1	100 $\mu$ g	€ 115
DuP-697	317500	A potent, irreversible, and time-dependent COX-2 inhibitor. Exhibits over 50-fold greater inhibitory potency against human and murine recombinant COX-2 ( $IC_{50}$ = 80 nM and 40 nM at 5 and 10 minutes, respectively) than COX-1 ( $IC_{50}$ = 9 $\mu$ M). <i>Purity:</i> $\geq$ 95% by HPLC. M.W. 411.3	5 mg	€ 159
Flurbiprofen	344079	A non-steroidal anti-inflammatory agent that acts as a potent cyclooxygenase inhibitor ( $IC_{50}$ = 5 nM for LPS-induced COX in human peripheral blood cells). Reduces A $\beta$ loads and Congo Red staining in APP+PS1 transgenic mice. <i>Purity:</i> $\geq$ 98% by titration. M.W. 244.3	100 mg	€ 39
Indomethacin Amide, N-Octyl-	405270	An N-octylamide derivative of Indomethacin (Cat. No. 405268) that acts as a potent and selective COX-2 inhibitor ( $IC_{50}$ = 40 nM) compared to COX-1 ( $IC_{50}$ = 66 $\mu$ M). <i>Purity:</i> $\geq$ 97% by HPLC. M.W. 469	5 mg	€ 110
Indomethacin Ester, n-Heptyl-	405269	A heptyl ester derivative of Indomethacin (Cat. No. 405268) that acts as a potent and selective COX-2 inhibitor ( $IC_{50}$ = 40 nM) compared to COX-1 ( $IC_{50}$ >66 $\mu$ M). <i>Purity:</i> $\geq$ 97% by HPLC. M.W. 456	5 mg	€ 110
Indomethacin Ester, 4-Methoxyphenyl-	405271	A 4-methoxyphenyl ester derivative of Indomethacin (Cat. No. 405268) that acts as a potent and selective COX-2 inhibitor ( $IC_{50}$ = 40 nM) compared to COX-1 ( $IC_{50}$ >66 $\mu$ M). <i>Purity:</i> $\geq$ 97% by HPLC. M.W. 463.9	5 mg	€ 110
Meloxicam	444800	Preferentially inhibits COX-2 ( $IC_{50}$ = 4.7 $\mu$ M) relative to COX-1 ( $IC_{50}$ = 36.6 $\mu$ M). <i>Purity:</i> $\geq$ 98% by HPLC. M.W. 351.4	100 mg	€ 123
Niflumic Acid	481987	A selective inhibitor of COX-2 ( $K_i$ = 20 nM for sheep placental COX-2). <i>Purity:</i> $\geq$ 98% by TLC. M.W. 282.2	1 g	€ 37
NS-398	349254	Selective inhibitor of COX-2 ( $IC_{50}$ = 3.8 $\mu$ M for sheep placental COX-2). Reduces neuronal damage following a stroke. <i>Purity:</i> $\geq$ 98% by TLC. M.W. 314.4	5 mg	€ 109

### MIF Antagonist, ISO-1

[(S,R)-3-(4-Hydroxyphenyl)-4,5-dihydro-5-isoxazole acetic acid, methyl ester; Macrophage Migration Inhibitory Factor Antagonist, ISO-1]

A cell-permeable anti-inflammatory, antidiabetogenic agent that inhibits MIF tautomerase activity by binding to its catalytic active site ( $IC_{50}$  = 7  $\mu$ M for D-dopachrome tautomerase) and suppresses the production of TNF- $\alpha$ , PGE<sub>2</sub>, and COX-2 in human monocytes, and arachidonic acid in RAW 264.7 macrophages. *Purity:*  $\geq$ 95% by HPLC. M.W. 235.1



Cat. No. 475837      5 mg      € 98

Ref.: Cvetkovic, I., et al. 2005. *Endocrinology*, 146, 2942; Lubetsky, J.B., et al. 2002. *J. Biol. Chem.* 277, 24976.

## Interested in SOD Detection?

### Superoxide Dismutase Assay Kit II

A convenient colorimetric assay for all three types of superoxide dismutase (Cu/Zn, Mn, and Fe) in plasma, serum, cell lysates, and tissue homogenates. Assay Range: 0.025-0.25 units per ml SOD.

Cat. No. 574601      1 kit      € 459

### Also Available...

#### Superoxide Dismutase, Human, Recombinant, *E. coli*

Recombinant human superoxide dismutase expressed in *E. coli* and purified by proprietary chromatographic methods. Activity:  $\geq$ 5000 units/mg. *Purity:*  $\geq$ 90% by SDS-PAGE. M.W. 31,608

Cat. No. 574591      100  $\mu$ g      € 284

## Looking for Antibodies to mTOR and TORC?

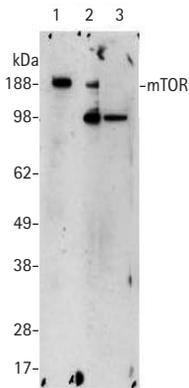
### Anti-mTOR/FRAP (Ab-2) Mouse mAb (22C2)

Liquid, Protein G purified. Immunogen used was a synthetic peptide corresponding to amino acids 230-240 of human TOR. Recognizes the ~290 kDa mTOR protein in HEK293 cells. Reacts with human. IB, IP

Cat. No. OP97                      100 µg                      € 285

### PhosphoDetect™ Anti-mTOR (pSer<sup>2448</sup>) Rabbit pAb

Liquid, immunoaffinity purified. Immunogen used was a synthetic phosphopeptide corresponding to amino acids surrounding Ser<sup>2448</sup> in human TOR. Detects ~290 kDa mTOR protein phosphorylated on Ser<sup>2448</sup> in EGF-treated HEK293 cells. Reacts with human. IB



Detection of human TOR, phosphorylated at Ser<sup>2448</sup> by immunoblotting. Samples: Cell lysates (50 µg) from EGF-treated HEK293 cells incubated without λ phosphatase (lanes 1, 2) or with λ phosphatase (Cat. No. 539514). Primary antibody: PhosphoDetect™ Anti-mTOR (pSer<sup>2448</sup>) Rabbit pAb (3 µg/ml). Detection: chemiluminescence.

Cat. No. PS1020                      50 µg                      € 154

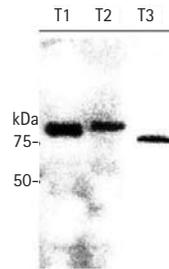
### Anti-TORC2 (454-607) Rabbit pAb

Liquid, undiluted serum. Immunogen used was a recombinant protein containing amino acids 454-607 of mouse TORC2 fused to GST. Recognizes the ~79-85 kDa TORC2 protein in primary hepatocytes. Reacts with human, mouse, and rat. IB, IP

Cat. No. ST1099                      50 µl                      € 122

### Anti-PAN TORC (1-42) Rabbit pAb

Liquid, undiluted serum. Immunogen used was a recombinant protein containing amino acids 1-42 of human TORC1 fused to GST. Recognizes the ~79 kDa TORC1, TORC2, and TORC3 proteins in 293T cells over-expressing TORC1, TORC2, or TORC3. Recognizes endogenous TORC1 and TORC2. Reacts with human, mouse, and rat. IB, IP



Detection of human TORC1, 2, and 3 by immunoblotting. Samples: FLAG-tagged recombinant TORC1 (T1), TORC2 (T2), and TORC3 (T3) immunoprecipitates from over expressing 293T cells using anti-FLAG antibody. Primary antibody: Pan-TORC (1-42) Rabbit pAb (Cat. No. ST1098) (1:2000). Detection: chemiluminescence.

Cat. No. ST1098                      50 µl                      € 122

## Introducing... **NEW** Protein Phosphatase Inhibitor Cocktail Sets

Add Convenience and Consistency to your research

### Phosphatase Inhibitor Cocktail Set III

A cocktail of four phosphatase inhibitors for broad-spectrum inhibition of acid phosphatases, serine/threonine phosphatases, and protein tyrosine phosphatases. Each vial contains 1 ml of aqueous solution with the following components: 50 mM Sodium Fluoride, 10 mM β-Glycerophosphate (Cat. No. 356756), 10 mM Sodium Pyrophosphate Decahydrate, 1 mM Sodium Orthovanadate.

Cat. No. 524627                      1 ml                      € 104  
1 set (5 x 1 ml)                      € 356

### Phosphatase Inhibitor Cocktail Set IV

A cocktail of three phosphatase inhibitors for the inhibition of serine/threonine and alkaline phosphatases. Each vial contains a 1 ml solution with the following components: 500 µM Cantharidin (Cat. No. 210155), 2.5 mM (-)-p-Bromotetramisole oxalate, and 1 µM Calyculin A, *Discodermia calyx* (Cat. No. 208851).

Cat. No. 524628                      1 ml                      € 68  
1 set (5 x 1 ml)                      € 257

## **NEW** Heat Shock Protein

### Hsp90β, His•Tag®, Human, Recombinant

Human full-length Hsp90β with an N-terminal His•Tag® sequence expressed in and purified from *Spodoptera frugiperda* insect cells.

Cat. No. 385903                      20 µg                      € 157

Ref.: Prodromou, C. and Pearl, L.H. 2003. *Curr. Cancer Drug Targets* 3, 301.

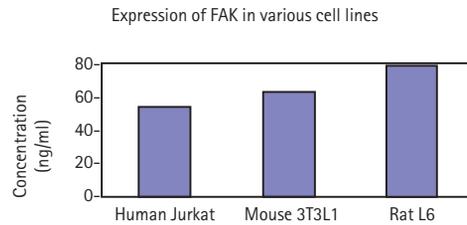
# Protein Kinase Assay Kits

## FAK ELISA Kit

A 96-well-based solid phase sandwich ELISA kit for quantitation of focal adhesion kinase (FAK). Detects FAK independent of its phosphorylation state in human, mouse and rat cells. Does not exhibit any cross-reactivity with several other protein kinases tested.

Sensitivity: < 1.6 ng/ml; Assay Range: 1.6-100 ng/ml.

Cat. No. CBA063      1 kit      € 518

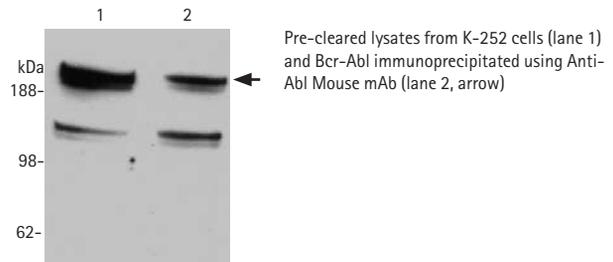


Whole cell lysates (200 µg/ml) from Jurkat cells, 3T3L1, and L6 cells were analyzed for total FAK.

## IP-Activity™ Bcr-Abl/c-Abl Kit

Designed to immunoprecipitate Abl tyrosine kinase from a variety of samples including cell lysates and partially purified preparations. Immunoprecipitated Abl retains activity and can be used in activity and inhibitor assays as well as immunoblots.

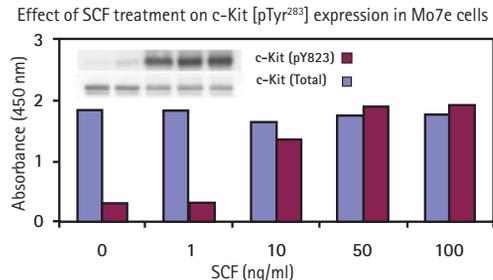
Cat. No. CBA052      1 kit      € 135



## c-Kit ELISA Kit

A 96-well solid phase sandwich ELISA suitable for detection and quantification of human c-Kit protein independent of its phosphorylation state. c-Kit binds to the immobilized monoclonal antibody specific for c-Kit. After washing, a rabbit polyclonal antibody specific for c-Kit is added that serves as a detection antibody. Anti-rabbit IgG-HRP is used for detection.

Cat. No. CBA074      1 kit      € 518

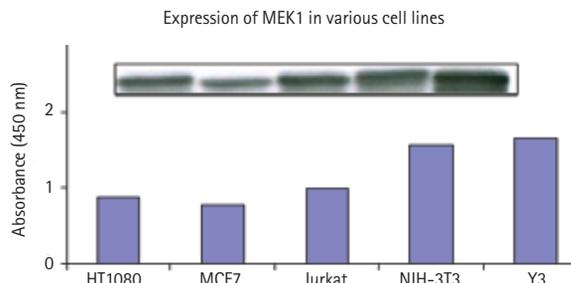


Mo7e cells treated with stem cell factor (SCF; 1-100 ng/ml) for 10 minutes were lysed and quantified in parallel for total c-Kit and c-Kit (pTyr<sup>823</sup>) expression. The total c-Kit remains constant, but the level of phosphorylation at Tyr<sup>823</sup> is increased following SCF treatment. Results correlate well with Western blot analysis.

## MEK1 ELISA Kit

A 96-well solid phase sandwich ELISA for detection and quantification of MEK1 independent of its phosphorylation state in human, mouse, and rat cells. MEK1 simultaneously binds to a monoclonal antibody specific for MEK1 (regardless of its phosphorylation state) and to a solution phase rabbit polyclonal detection antibody that is specific for MEK1. After washing, anti-rabbit IgG-HRP is added that binds to the detection antibody.

Cat. No. CBA070      1 kit      € 518

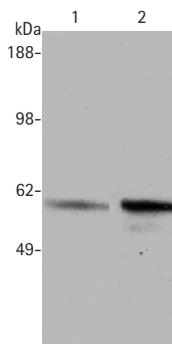


Detection of MEK1 in human (HT1080; MCF-7; Jurkat), mouse (NIH-3T3), and rat (Y3) cell lysates. The levels of MEK1 protein detected with this kit are consistent with results obtained by Western blotting.

## IP-Activity™ Src Kit

Designed to immunoprecipitate c-Src and v-Src tyrosine kinase from a variety of sources, including cell lysates and partially purified preparations. The Src/Protein G complex retains kinase activity and can be used directly to evaluate Src activity.

Cat. No. CBA056      1 kit      € 135



Immunoprecipitation of c-Src from A431 cell lysates. Lane 1: Pre-cleared lysates. Lane 2: immunoprecipitate using Anti-c-Src Mouse mAb (357).

## NEW Antibodies for Protein Kinases

Name	Cat. No.	Comments	Size	Price
Anti-PAK6 Rabbit pAb	ST1108	Liquid, immunoaffinity purified. Immunogen used was a synthetic peptide corresponding to an internal sequence of human PAK6. Recognizes the ~80 kDa PAK6 protein in transiently transfected CHO cells. Reacts with human. <b>IB, IP</b>	50 µg	€ 122
PhosphoDetect™ Anti-c-Abl (pTyr <sup>245</sup> ) Rabbit pAb	PK1013	Liquid, protein A and immunoaffinity purified. Immunogen used was a synthetic phosphopeptide corresponding to amino acids surrounding the Tyr <sup>245</sup> phosphorylation site of human c-Abl, coupled to KLH. Recognizes the ~135 kDa c-Abl phosphorylated at Tyr <sup>245</sup> in HEK293 cells over-expressing constitutively active c-Abl. Also recognizes the ~210 kDa form of Bcr-Abl phosphorylated at Tyr <sup>245</sup> in K562 cells. Reacts with human and mouse. <b>IB</b>	50 µl	€ 176
PhosphoDetect™ Anti-c-Abl (pThr <sup>735</sup> ) Rabbit pAb	PK1006	Liquid, protein A and immunoaffinity purified. Immunogen used was a synthetic phosphopeptide corresponding to amino acids surrounding the Thr <sup>735</sup> phosphorylation site of human c-Abl coupled to KLH. Recognizes the ~145 kDa c-Abl and the ~190 kDa and ~210 kDa forms of Bcr-Abl phosphorylated at Thr <sup>735</sup> in sorbitol-treated HeLa cells. Reacts with human. <b>IB</b>	50 µl	€ 176
PhosphoDetect™ Anti-p70S6K(pThr <sup>389</sup> ) Rabbit pAb	PK1015	Liquid, immunoaffinity purified. Immunogen used was a synthetic phosphopeptide corresponding to amino acids surrounding the Thr <sup>389</sup> phosphorylation site of human p70S6K. Recognizes the ~60 kDa p70S6 kinase protein phosphorylated on Tyr <sup>389</sup> in MCF7 cells. Reacts with human. <b>ELISA, IB</b>	50 µg	€ 122
Anti-Chk2 Rabbit pAb	DR1036	Liquid, undiluted serum. Immunogen used was a full-length, human, recombinant Chk2 protein expressed in insect cells with a His*Tag® sequence. Recognizes the ~62 kDa Chk2 protein in HeLa cells. Reacts with human. <b>IB, IP</b>	50 µl	€ 122
PhosphoDetect™ Anti-VEGFR2 (pTyr <sup>1214</sup> ) Rabbit pAb	PS1012	Liquid, immunoaffinity purified. Immunogen used was a synthetic phosphopeptide corresponding to amino acids surrounding the Tyr <sup>1214</sup> phosphorylation site of human VEGFR-2. Recognizes the ~200 kDa VEGFR-2 phosphorylated at Tyr <sup>1214</sup> . Reacts with human and mouse. <b>IB</b>	10 T	€ 295
PhosphoDetect™ Anti-VEGFR2 (pTyr <sup>1054/1059</sup> ) Rabbit pAb	PS1013	Liquid, immunoaffinity purified. Immunogen used was a synthetic phosphopeptide corresponding to amino acids surrounding the Tyr <sup>1054/1059</sup> phosphorylation sites of human VEGFR-2. Recognizes the ~200 kDa VEGFR-2 protein phosphorylated at Tyr <sup>1054/1059</sup> in porcine pancreatic cells transfected with a CSF-1/mouse VEGFR-2 chimeric receptor. Reacts with mouse. <b>IB</b>	100 µl	€ 295
PhosphoDetect™ Anti-Syk (pTyr <sup>525/526</sup> ) Rabbit pAb	PK1010	Liquid, protein A and immunoaffinity purified. Immunogen used was a synthetic phosphopeptide corresponding to amino acids surrounding the Tyr <sup>525/526</sup> phosphorylation site of human Syk. Recognizes the ~72 kDa Syk protein phosphorylated at Tyr <sup>525/526</sup> in human Syk and Tyr <sup>519/520</sup> in mouse Syk in 293T cells expressing wild-type Syk and CD8. Reacts with human and mouse. <b>ELISA, IB</b>	50 µl	€ 176

ELISA: enzyme-linked immunosorbent assay; IB: immunoblotting; IP: immunoprecipitation; 10 T: 10 tests by Western miniblott



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## **NEW** Recombinant Protein Kinases

### CSK, GST-Fusion Protein, Active, Human, Recombinant, *S. frugiperda*

Full-length, human, recombinant CSK (Genbank accession number = NM\_004383) expressed as a GST fusion protein (N-terminal) in Sf9 insect cells using a baculovirus expression system. *Specific activity*:  $\geq 362$  nmol/min/mg protein. *Purity*:  $>85\%$  by SDS-PAGE

**Cat. No. 235706**      **5 µg**      **€ 90**

Ref.: Cloutier, J. F. and Veillette, A. 1996. *EMBO J.* 15, 4909; Armstrong, E., et al. 1992. *Cytogenet. Cell Genet.* 60, 119; Partanen, J., et al. 1991. *Oncogene* 6, 2013.

### MAPKAP Kinase 3, GST-Fusion Protein, Active, Human, Recombinant, *S. frugiperda*

(Mitogen-activated protein kinase-activated protein 3, GST-Fusion Protein, Human, Recombinant)

Full-length, recombinant, human mitogen-activated protein kinase-activated protein 3 (MAPKAPK 3)(GenBank accession number = NM\_004635) fused to GST at the N-terminus. *Specific activity*:  $\geq 540$  nmol/min/mg. *Purity*:  $\geq 90\%$  by SDS-PAGE

**Cat. No. 475862**      **5 µg**      **€ 135**

Ref.: Maizels, E.T., et al. 2001. *Mol. Endocrinol.* 15, 716; Neufeld, B., et al. 2000. *J. Biol. Chem.* 275, 20239; Ludwig, S., et al. 1996. *Mol. Cell. Biol.* 16, 6687; Sithanandam, G., et al. 1996. *Mol. Cell. Biol.* 16, 868.

### p38δ, GST-Fusion Protein, Active, Human, Recombinant, *S. frugiperda*

Full-length, recombinant, human p38δ/SAPK4 (Genbank accession number = NM\_002754) fused at the N-terminus to GST. *Specific activity*:  $\geq 220$  nmol/min/mg. *Purity*:  $\geq 80\%$  by SDS-PAGE

**Cat. No. 559325**      **5 µg**      **€ 135**

Ref.: Goedert, M., et al. 1997. *EMBO J.* 16, 3563; Kumar, S., et al. 1997. *Biochem. Biophys. Res. Commun.* 235, 533.

### PKC<sub>ε</sub>, GST-Fusion Protein, Active, Human, Recombinant, *S. frugiperda*

Full-length, recombinant, human PKC<sub>ε</sub> (Genbank accession number = NM\_005400) fused at the N-terminus to GST. *Specific activity*:  $\geq 1000$  nmol/min/mg. *Purity*:  $>90\%$  by SDS-PAGE

**Cat. No. 539691**      **5 µg**      **€ 90**

Ref.: Baines, C.P., et al. 2003. *Circ. Res.* 92, 873; Hodge, C.W., et al. 2002. *J. Clin. Invest.* 110, 1003; Premkumar, L.S. and Ahern, G.P. 2000. *Nature* 408, 985; Chen, C.H., et al. 1999. *Proc. Natl. Acad. Sci. USA* 96, 12784; Knauf, J.A., et al. 1999. *J. Biol. Chem.* 274, 23414.

### Plk1, Human, Recombinant, *S. frugiperda* (Polo-like kinase 1, Human, Recombinant)

Human recombinant Polo-Like Kinase 1 (Plk1) expressed in insect cells using a baculovirus expression system. *Purity*:  $\geq 95\%$  by SDS-PAGE

**Cat. No. 346102**      **5000 U**      **€ 311**

Ref.: Liu, X. and Erikson, R. L. 2003. *Proc. Natl. Acad. Sci. U.S.A.* 100, 5789; Smith, M. R., et al. 1997. *Biochem. Biophys. Res. Commun.* 234, 397; Hamanaka, R., et al. 1994. *Cell Growth Differ.* 5, 249.

## **NEW** Protein Kinase Inhibitors

### InSolution™ Akt Inhibitor VIII, Isozyme-Selective, Akti-1/2

Supplied as a 10 mM (1 mg/181 µl) solution of Akt Inhibitor VIII, Isozyme-Selective, Akti-1/2 (Cat. No. 124018 in DMSO. *Purity*:  $\geq 95\%$  by HPLC.M.W. 551.6

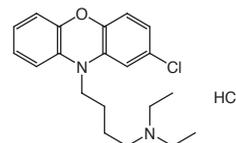
**Cat. No. 124017**      **1 mg**      **€ 117**

Ref.: Barnett, S.F., et al. 2005. *Biochem. J.* 385, 399; DeFeo-Jones, D., et al. 2005. *Mol. Cancer Ther.* 4, 271; Zhao, Z., et al. 2005. *Bioorg. Med. Chem. Lett.* 15, 905; Lindsley, C.W., et al. 2005. *Bioorg. Med. Chem. Lett.* 15, 761.

### Akt Inhibitor X

[10-(4'-(N-diethylamino)butyl)-2-chlorophenoxazine, HCl]

A cell-permeable, selective inhibitor of the phosphorylation of Akt and its *in vitro* kinase activity (complete inhibition  $< 5$  µM) with minimal effect on PI 3-K, PDK1, or SGK1. Unlike Akt-1/2 (Cat. No. 124018), the mode of inhibition is not PH domain-dependent. *Purity*:  $\geq 95\%$  by HPLC.M.W. 381.4



**Cat. No. 124020**      **5 mg**      **€ 176**

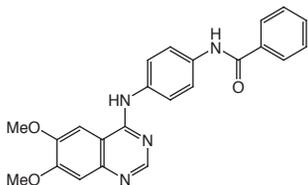
Ref.: Thimmaiah, K.N., et al. 2005. *J. Biol. Chem.* 280, 31924.

# Protein Kinase Inhibitors (continued...)

## Aurora Kinase Inhibitor II

[4-(4'-Benzamidoanilino)-6,7-dimethoxyquinazoline]

A cell-permeable, potent, selective, and ATP-competitive inhibitor of Aurora kinases ( $IC_{50}$  = 310 nM and 240 nM for Aurora A and B, respectively, 1.25  $\mu$ M in MCF7 cells). Due to its limited aqueous solubility and high serum binding property, it is recommended for *in vitro*, but not *in vivo*, use. *Purity*:  $\geq 97\%$  by HPLC. M.W. 400.4



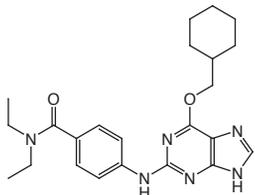
Cat. No. 189404      1 mg      € 77

Ref.: Heron, N.M., et al. 2006. *Bioorg. Med. Chem. Lett.* 16, 1320; Mortlock, A.A., et al. 2005. *Curr. Top. Med. Chem.* 5, 807.

## Cdk2 Inhibitor IV, NU6140

[4-(6-Cyclohexylmethoxy-9H-purin-2-ylamino)-N,N-diethylbenzamide]

A highly cell-permeable, selective, ATP-competitive inhibitor of Cdks ( $IC_{50}$  = 6.6  $\mu$ M, 0.41  $\mu$ M, 5.5  $\mu$ M, 15  $\mu$ M and 3.9  $\mu$ M for Cdk1/cyclin B, Cdk2/cyclin A, Cdk4/cyclin D, Cdk5/p25 and Cdk7/cyclin H, respectively). Shown to cause cell cycle arrest at the  $G_2/M$  phase and induce apoptosis by activating caspases and down-regulating survivin. *Purity*:  $\geq 95\%$  by HPLC. M.W. 422.5



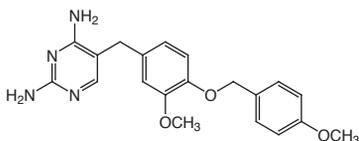
Cat. No. 238804      5 mg      € 122

Ref.: Pennati, M., et al. 2005. *Mol. Cancer Ther.* 4, 1328.

## cFMS Receptor Tyrosine Kinase Inhibitor

[CSF-1 Receptor Inhibitor; 5-(3-Methoxy-4-((4-methoxybenzyl)oxy)benzyl)-pyrimidine-2,4-diamine]

A cell-permeable, potent, selective, and ATP-competitive inhibitor of cFMS kinase ( $IC_{50}$  = 30 nM) with minimal inhibition towards a panel of 26 other kinases ( $IC_{50}$  > 5  $\mu$ M). *Purity*:  $\geq 97\%$  by HPLC. M.W. 366.4



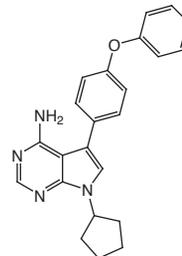
Cat. No. 344036      1 mg      € 72

Ref.: Conway, J.G., et al. 2005. *Proc. Natl. Acad. Sci. USA* 102, 16078.

## Lck Inhibitor

{4-Amino-5-(4-phenoxyphenyl)-7H-pyrrolo[3,2-d]pyrimidin-7-yl-cyclopentane}

A cell-permeable, potent, selective, and ATP-competitive inhibitor of Lck ( $IC_{50}$  at 5  $\mu$ M ATP = < 1 nM, 2 nM, 70 nM, 1.57  $\mu$ M and 1.98  $\mu$ M for Lck<sub>64-509</sub> Y<sup>394</sup>, Lckcd pY<sup>394</sup>, Src, Kdr and Tie-2, respectively;  $IC_{50}$  at 1 mM ATP = 16  $\mu$ M, 66 nM, 126 nM, 420 nM, and 5.18  $\mu$ M for Lck<sub>64-509</sub> Y<sup>394</sup>, Blk, Fyn, Lyn, and Csk, respectively). *Purity*:  $\geq 95\%$  by HPLC, M.W. 370.5



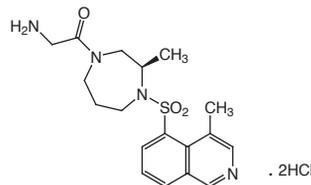
Cat. No. 428205      1 mg      € 72

Ref.: Burchat, A.F., et al. 2000. *Bioorg. Med. Chem. Lett.* 10, 2171; Arnold, L.D., et al. 2000. *Bioorg. Med. Chem. Lett.* 10, 2167.

## Rho Kinase Inhibitor IV

[H-1152, Glycyl; (S)-(+)-2-Methyl-4-glycyl-1-(4-methylisoquinolinyl-5-sulfonyl)homopiperazine, 2HCl]

A glycyl analog of Rho-Kinase Inhibitor (Cat. No. 555550) that inhibits ROCK with an improved selectivity ( $IC_{50}$  = 11.8 nM, > 10  $\mu$ M, > 10  $\mu$ M, 3.26  $\mu$ M, 2.35  $\mu$ M, and 2.57  $\mu$ M for ROCKII, PKA, PKC, PKG, Aurora A, and CaMKII, respectively). *Purity*:  $\geq 98\%$  by HPLC. M.W. 467.4



Cat. No. 555554      1 mg      € 135

Ref.: Tamura, M., et al. 2005. *Biochim. Biophys. Acta*, 1754, 245.

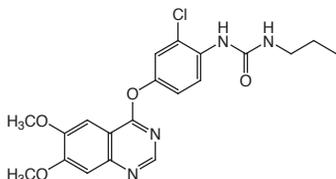
## Protein Kinase Inhibitors (continued...)

### VEGF Receptor Tyrosine Kinase Inhibitor III, KRN633

[N-(2-Chloro-4-((6,7-dimethoxy-4-quinazolinyloxy)phenyl)-N'-propylurea]

A cell-permeable, reversible, ATP-competitive inhibitor of VEGFR kinase activity ( $IC_{50}$  = 170 nM, 160 nM, and 125 nM for VEGFR-1, VEGFR-2, VEGFR-3, respectively). Inhibits PDGFR- $\alpha$  and c-Kit only at higher concentrations ( $IC_{50}$  = 970 nM and 4.33  $\mu$ M, respectively) and is inactive towards a panel of 17 other kinases ( $IC_{50}$   $\geq$  10  $\mu$ M).

Purity:  $\geq$ 97% by HPLC.M.W. 416.9



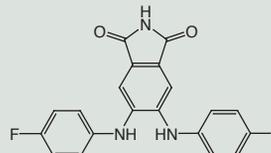
Cat. No. 676482      1 mg      € 122

Ref.: Nakamura, K., et al. 2004. *Mol. Cancer Ther.* 3, 1639.

### PKC $\beta$ II/EGFR Inhibitor

[4,5-bis(4-Fluoroanilino)-phthalimide; CG53353; CGP 53 353; DAPH 2]

A cell-permeable, potent, ATP-competitive inhibitor of EGFR and PKC isozymes  $\alpha$ ,  $\beta$ I, and  $\beta$ II ( $IC_{50}$  = 700 nM, 1.9  $\mu$ M, 3.8  $\mu$ M, and 410 nM, respectively). Only weakly inhibits the activity of a panel of 16 other kinases, including novel and atypical PKC isozymes. Reported to inhibit insulin-stimulated cellular 2-deoxyglucose uptake, osteoclast differentiation, ERK activation, and TLS/FUS DNA-binding activity *in vitro*. Purity:  $\geq$ 98% by HPLC.M.W. 365.3



Cat. No. 539652      2 mg      € 99

Ref.: Kouroedov, A., et al. 2004. *Circulation* 110, 91; Lee, S.W., et al. 2003. *Bone* 32, 217; Perrotti, D., et al. 1998. *EMBO J.* 17, 4442; Chalfant, C.E., et al. 1996. *Mol. Endocrinol.* 10, 1273; Buchdunger, E., et al. 1995. *Clin. Cancer Res.* 1, 813; Trinks, U., et al. 1994. *J. Med. Chem.* 37, 1015.

## **NEW** Bone Morphogenetic Proteins

Bone morphogenetic proteins (BMPs) are a group of developmental regulatory factors of the transforming growth factor- $\beta$  superfamily. They are produced by osteoblasts and other bone cells and affect osteoblast proliferation and differentiation. All BMPs share a high degree of sequence homology. BMPs elicit their responses through activation of membrane associated BMP receptors type-IA, -IB, and -II, which in turn activate Smad molecules that translocate to the nucleus and cause transcriptional activation.

### BMP-2, Human, Recombinant, *E. coli*

A disulfide-bonded homodimeric protein that plays an important role in cardiac morphogenesis. Lyophilized from a sterile solution containing 10 mM sodium citrate, pH 3.5. *Biological activity*:  $ED_{50}$  <50 ng/ml based on the cytolysis of MCT3T3-E1 cells. *Purity*:  $\geq$ 95% by RP-HPLC.

Cat. No. 203641      2  $\mu$ g      € 113

### BMP-4, Human, Recombinant, *E. coli*

A monomeric protein that plays an important role in the development of various organs and is essential for bone growth and regeneration in periodontal tissue. Suitable for use as a standard in Western blotting and for generating BMP-4 monomer antibodies. *Purity*:  $\geq$ 95% by RP-HPLC.

Cat. No. 203642      2  $\mu$ g      € 113

### BMP-6, Human, Recombinant, *E. coli*

A homodimeric osteogenic protein that induces phosphorylation and nuclear accumulation of Smad5 and serves as a positive regulator of keratinocyte differentiation. Suitable for use as a standard in Western blotting and for generating BMP-6 antibodies. *Purity*:  $\geq$ 95% by RP-HPLC.

Cat. No. 203643      2  $\mu$ g      € 113

### BMP-7, Human, Recombinant, *E. coli*

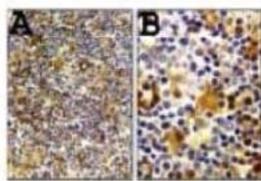
A monomeric protein that plays an important role in embryogenic renal and eye development. Suitable for use as a standard in Western blotting and for generating BMP-7 antibodies. *Purity*:  $\geq$ 95% by RP-HPLC.

Cat. No. 203645      2  $\mu$ g      € 113

## NEW Tools for Apoptosis Research

### Anti-Caspase-1 (31-45) Rabbit pAb

Liquid, Protein G purified. Immunogen used was a synthetic peptide corresponding to amino acids 31-45 of human caspase-1. Recognizes the ~45 kDa latent form of caspase-1 in HeLa cells. Reacts with human. **IB, PS**

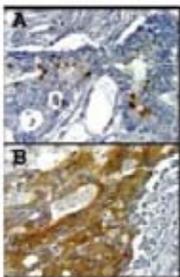


Detection of human caspase-1 by staining paraffin sections. Samples: Formalin-fixed lymph nodes. Primary antibody: Anti-Caspase-1 (31-45) Rabbit pAb (Cat. No. AP1044). Detection: DAB with hematoxylin counterstain.

Cat. No. AP1044      50 µg      € 149

### Anti-Caspase-1 Mouse mAb (14F468)

Liquid, purified. Immunogen used was a synthetic peptide corresponding to amino acids 371-390 of human caspase-1. Recognizes the ~45 kDa latent form of caspase-1 in HeLa and NIH3T3 cells. Also recognizes cleaved forms of caspase-1 that retain amino acids 371-390. Reacts with human and mouse. **IB, PS**



Detection of human caspase-1 by staining paraffin sections. Sample: Colon carcinoma, formalin fixed (panels A and B). Primary antibody: Anti-Caspase-1 Mouse mAb (14F468) (Cat. No. AP1043). Detection: DAB with hematoxylin counterstain.

Cat. No. AP1043      50 µg      € 167

### MDM2, Human, Recombinant, *E. coli* (Mouse Double Minute 2, Human, Recombinant, *E. coli*)

Recombinant, human MDM2 expressed in *E. coli* and purified by affinity chromatography using FPLC. Useful for *in vitro* transcription assays and DNA-protein and protein interaction assays. MDM2 (Mouse Double Minute 2) is an E3 ubiquitin ligase that was first identified in mouse as a small acentromeric extrachromosomal element. It was then shown to become oncogenic upon amplification and tumorigenic when overexpressed in NIH3T3 and Rat2 cells. MDM2 overexpression is known to promote tumor development by inhibiting wild-type p53 transcriptional activation. *Purity*: >95% by SDS-PAGE.

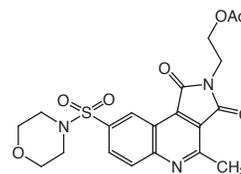
Cat. No. 444146      10,000 U      € 311

Ref.: Dornan, D., et al. 2004. *Nature* 429, 86; Chen, J., et al., 1996. *Mol. Cell. Biol.* 16, 2445; Gorgoulis, V.G., et al. 1996. *J. Pathol.* 180, 129; Finlay, C. A. 1993. *Mol. Cell. Biol.* 13, 301; Leach, F. S., et al. 1993. *Cancer Res.* 53, 2231; Oliner, J. D., et al. 1993. *Nature* 362, 857; Momand, J., et al. 1992. *Cell* 69, 1237; Oliner, J. D., et al. 1992. *Nature* 358, 80; Fakharzadeh, S. et al. 1991. *EMBO J.* 10, 1565.

### Caspase-3 Inhibitor VII

{2-(4-Methyl-8-(morpholin-4-ylsulfonyl)-1,3-dioxo-1,3-dihydro-2H-pyrrolo[3,4-c]quinolin-2-yl)ethyl acetate}

A cell-permeable, potent, reversible, and non-competitive inhibitor of caspase-3 ( $IC_{50} = 23$  nM). Displays higher anti-apoptotic activity than Z-VAD-FMK (Cat. No. 627610) in a model of Staurosporine (Cat. No. 569397) induced apoptosis in human Jurkat T cells. *Purity*: ≥97% by HPLC. M.W. 447.5



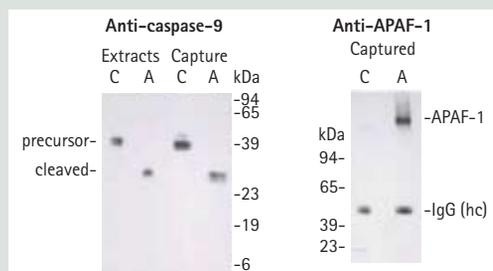
Cat. No. 219012      1 mg      € 122

Ref.: Kravchenko, D.V., et al. 2005. *J. Med. Chem.* 48, 3680.

### Active Caspase-9 Assay Kit

A 96-well based convenient immunofluorescent assay for the quantitative detection of active caspase-9 in cell lysates. The kit is based on capture of caspase-9 in complex with APAF-1. Active caspase-3 cleaves the prodomain of caspase-3 and activates it. Subsequent cleavage of DEVD-AFC by caspase-3 generates fluorescence (Ex. Max: 400 nm; Em. Max: 505 nm).

Cat. No. CBA047      1 kit      € 383



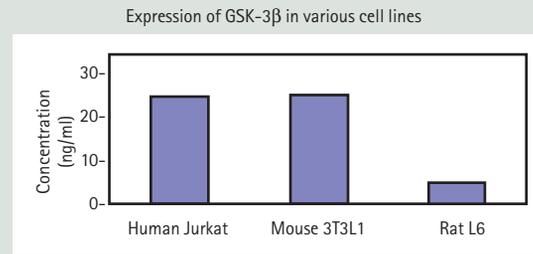
Caspase-9 complexed with APAF-1 is captured in this assay kit. Jurkat cell extracts were activated for 60 minutes at 30°C with cytochrome c and dATP (A) or with buffer only (C). Extracts were incubated in plate wells coated with caspase-9 capture antibody for 2 h. Wells were washed and captured proteins were solubilized in SDS sample buffer. Immunoblotting of extracts and captured proteins was performed using an anti-caspase-9 antibody or an anti-APAF-1 (Cat. No. AP1038).

# Neurochemical Corner

## GSK-3 $\beta$ ELISA Kit

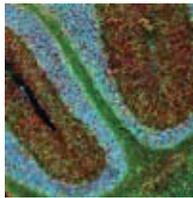
A 96-well solid phase sandwich ELISA for detection and quantification of GSK-3 $\beta$  protein independent of its phosphorylation state in human, mouse, and rat cells. GSK-3 $\beta$  is captured by anti-GSK-3 $\beta$  Mouse mAb coated on the plate. The antigen binds simultaneously to the capture antibody and to the detection antibody Anti-GSK-3 $\beta$  rabbit pAb. After washing anti-rabbit-IgG-HRP is added that binds to the detection antibody. Sensitivity: <0.26 ng/ml. Assay time: 4 h

Cat. No. CBA068      1 kit      € 518



## Anti-Neurofilament H Non-Phosphorylated Mouse mAb (SMI-32)

Liquid, undiluted ascites. Immunogen used was homogenized hypothalamic extract from Fischer 344 rats. Recognizes the non-phosphorylated ~180-200 kDa neurofilament H protein in rat CNS cytoskeletal preparations. Reacts with most mammalian species. ELISA, FS, IB, IC, PS

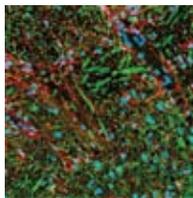


Detection of non-phosphorylated rat neurofilament H by staining frozen rat brain sections. Primary antibody: Anti-Neurofilament H Non-phosphorylated Mouse mAb (SMI-32) (Cat. No. NE1023)(1:1000). Detection: fluorescence (green) with Hoechst 33342 counterstain.

Cat. No. NE1023      100  $\mu$ l      € 275

## PhosphoDetect™ Anti-Neurofilament-H Mouse mAb (SMI-31)

Liquid, undiluted ascites. Immunogen used was homogenized hypothalamic extract from Fischer 344 rats. Recognizes the ~180-200 kDa phosphorylated neurofilament H (NF-H) protein in rat CNS cytoskeletal preparations. Weakly recognizes phosphorylated NF-M protein. Reacts with chicken, mammalian, and *Xenopus*. ELISA, FS, IB, IC, PS

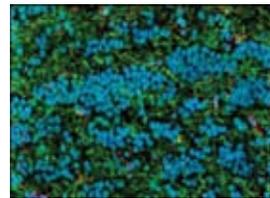


Detection of phosphorylated rat neurofilament H by staining frozen rat brain sections. Primary antibody: PhosphoDetect™ Anti-Neurofilament H Non-phosphorylated Mouse mAb (SMI-31) (Cat. No. NE1022)(1:1000). Detection: fluorescence (green) with Hoechst 33342 counterstain.

Cat. No. NE1022      100  $\mu$ l      € 275

## Anti-Pan-Axonal Neurofilament Marker Mouse mAb (SMI-312)

Liquid, undiluted ascites. Immunogen used was homogenized hypothalamic extract from Fischer 344 rats. Recognizes the ~180-200 kDa pan-axonal neurofilament marker in rat CNS cytoskeletal preparations. Reacts with most mammalian species. ELISA, FS, IB, IC, PS

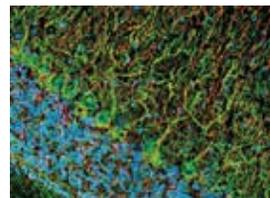


Detection of pan-axonal neurofilament marker by staining frozen rat brain sections. Primary antibody: Anti-Pan-Axonal Neurofilament Marker Mouse mAb (SMI-312) (Cat. No. NE1016)(1:1000). Detection: fluorescence (green) with Hoechst 33342 counterstain.

Cat. No. NE1016      100  $\mu$ l      € 275

## Anti-Pan-Neuronal Neurofilament Marker Mouse mAb (SMI-311)

Liquid, undiluted ascites. Immunogen used was homogenized hypothalamic extract from Fischer 344 rats. Recognizes ~180-200 kDa pan-neuronal neurofilament marker in rat CNS cytoskeletal preparations. Reacts with most mammalian species. ELISA, FS, IB, IC, PS

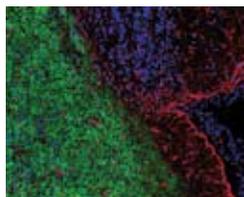


Detection of pan-neuronal neurofilament marker by staining frozen rat brain sections. Primary antibody: Anti-Pan-Neuronal Neurofilament Marker Mouse mAb (SMI-311) (Cat. No. NE1017)(1:1000). Detection: fluorescence (green) with Hoechst 33342 counterstain.

Cat. No. NE1017      100  $\mu$ l      € 275

### Anti-Microtubule Associated Protein 2 Mouse mAb (SMI-52)

Liquid, undiluted ascites. Immunogen used was bovine microtubule-associated protein 2. Recognizes the ~280 kDa MAP2a, MAP2b, and the ~68 kDa MAP2c protein in brain cytoskeletal preparations. Reacts with most mammalian species and *Xenopus*. ELISA, FS, IB, IC, PS

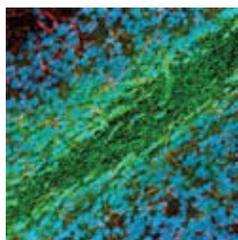


Detection of microtubule associated protein 2 by staining frozen rat brain sections. Primary antibody: Anti-Microtubule Associated Protein 2 Mouse mAb (SMI-52) (Cat. No. ST1110)(1:1000). Detection: fluorescence (green) with Hoechst 33342 counterstain.

Cat. No. ST1110 100 µl € 239

### Anti-Myelin Basic Protein Mouse mAb (SMI-94)

Liquid, undiluted ascites. Immunogen used was purified human myelin basic protein. Recognizes the ~21 kDa myelin basic protein (MBP) in rat brain extracts. Cross-reacts with canine, human, monkey, mouse, rabbit, and rat. ELISA, FS, IB, IC, PS.

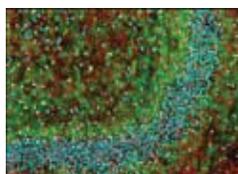


Detection of rat myelin basic protein by staining frozen sections. Primary antibody: Anti-Myelin Basic Protein Mouse mAb (SMI-94) (Cat. No. NE1018) (1:1000). Detection: fluorescence (green) with Hoechst counterstain.

Cat. No. NE1018 100 µl € 329

### Anti-Myelin Basic Protein Mouse mAb (SMI-99)

Liquid, undiluted ascites. Immunogen used was human myelin basic protein. Recognizes the ~21 kDa myelin basic protein brain extracts from most mammalian species. Does not react with porcine. Does not recognize the 14 kDa form ELISA, FS, IB, IC, PS.



Detection of rat myelin basic protein by staining frozen sections. Primary antibody: Anti-Myelin Basic Protein Mouse mAb (SMI-99) (Cat. No. NE1019) (1:1000). Detection: fluorescence (green) with Hoechst 33342 counterstain.

Cat. No. NE1019 100 µl € 239

### Anti-SNAP-25 (195-206) Rabbit pAb

Liquid, unpurified. Immunogen: a synthetic peptide (CANQRATKMLGSG) corresponding to amino acids 195-206 of mouse SNAP-25, with a cysteine (C) added and coupled to KLH. Recognizes the ~25 kDa SNAP-25 protein in mouse and rat brain tissue extracts. Reacts with mouse, rat. IB, IP

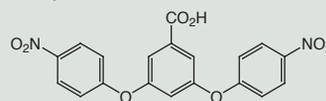
Cat. No. NE1014 100 µl € 266

### Secretase Modulator, CW

[CW; 3,5-bis(4-Nitrophenoxy)benzoic acid]

A cell-permeable inhibitor of  $A\beta_{42}$  and  $N\beta_{25}$  (Notch-1  $A\beta$ -like 25-mer peptide) secretion during presenilin (PS)-dependent intramembrane proteolysis in cells.

Purity:  $\geq 99\%$  by HPLC. M.W. 396.3



Cat. No. 234515 100 mg € 68

Ref.: Okochi, M., et al. 2006. *J. Biol. Chem.* 281, 7890.

## NEW Glycobiology Research Products

### Galectin-1, Human, Recombinant, *E. coli*

(14 kDa lectin; Galaptin; HBL; HPL;  $\beta$ -galactoside-binding lectin L-14-I; Lactose-binding lectin 1)

Recombinant human galectin-1 expressed in and purified from *E. coli*. Purity:  $\geq 98\%$  by SDS-PAGE.

Cat. No. 345831 50 µg € 225

Ref.: Rabinovich, A., et al. 2002. *Trends Immunol.* 23, 313; Rabinovich, A., et al. 2002. *J. Leukoc. Biol.* 71, 741; Hughes, R.C., et al. 2001. *Biochimie.* 83, 667.

### Galectin-3C, Human, Recombinant, *E. coli*

The mature form of human galectin-3 expressed in and purified from *E. coli* and subsequently cleaved with *Clostridium histolyticum* collagenase type VII to yield galectin-3C. The resulting galectin-3C is purified by affinity chromatography. Galectin-3C is a truncated form of galectin-3 that contains the carbohydrate binding domain but lacks the 107 amino acids at the N-terminus of galectin-3. Purity:  $\geq 95\%$  by SDS-PAGE.

Cat. No. 345832 100 µg € 401

Ref.: Hoyer K.K., et al. 2004. *Am. J. Pathol.* 164, 893; John C.M., et al. 2003. *Clin. Cancer Res.* 9, 2374; Iurisci, L., et al. 2000. *Clin. Cancer Res.* 6, 1389; Van Den Brule, F. A., et al. 2000. *Int. J. Cancer* 89, 361; Inohara, H. 1999. *Cancer* 85, 2475; Ochieng, J., et al. 1998. *Biochim. Biophys. Acta.* 1379 97; Castronovo, V., et al. 1996. *J. Pathol.* 179, 43; Massa, S.M., et al. 1993. *Biochemistry* 32, 260.

### InnoZyme™ Calpain1/2 Activity Assay Kit

Format: 96-well plate

Sample type: Cell lysates, tissues extracts

A highly sensitive and specific assay for measuring calpain 1 and 2 activity in biological samples like cell lysate or tissue extracts and for screening enzyme inhibitors. Calpains (calcium ion-dependent papain-like cysteine proteases) are widely distributed in all mammalian cells. They mediate calcium-induced activation of the Erk1/Erk2 MAPK pathway and are believed to participate in intracellular signal processing via limited proteolysis of their targets.

**Cat. No. CBA054                      1 kit                      € 315**

### Calpain-1 Substrate II, Fluorogenic

[H-E(EDANS)PLF~AERK(DABCYL)-OH]

An internally quenched peptide substrate that is optimized for calpain-1 amino acid recognition motifs at the primed as well as the non-primed sides. Shown to be kinetically superior, in terms of turnover rate, to Calpain Substrate III, Fluorogenic (Cat. No. 208771), Calpain-1 Substrate, Fluorogenic (Cat. No. 208748), and Calpain Substrate II, Fluorogenic (Cat. No. 208731) by ~8-, 18-, and 310-fold, respectively. *Purity: ≥97% by HPLC.*

M.W. 1488.7

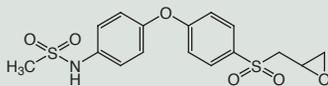
**Cat. No. 208772                      1 mg                      € 158**

Ref.: Cuerrier, D., et al. *J. Biol. Chem.* 280, 40632.

### MMP-2 Inhibitor II

[[4-(4-(Methanesulfonamido)phenoxy)phenylsulfonyl)methylloxirane]

An oxirane analog of SB-3CT, pMS (Cat. No. 444285) that acts as a selective, active site-binding, irreversible inhibitor of MMP-2 ( $K_i = 2.4 \mu\text{M}$ ). Although less potent, it exhibits enhanced selectivity towards MMP-2 ( $K_i = 45$  and  $379 \mu\text{M}$  for MMP-1 and MMP-7, respectively) than SB-3CT, pMS. *Purity: ≥97% by HPLC.* M.W. 383.4



**Cat. No. 444286                      5 mg                      € 126**

Ref.: Ikejiri, M., et al. 2005. *J. Biol. Chem.* 280, 33992.

### MMP-2/MMP-9 Inhibitor V

[[4-(4-(Methanesulfonamido)phenoxy)phenylsulfonyl)methylthiirane; SB-3CT, pMS]

A cell-permeable sulfonamido analog of SB-3CT (Cat. No. 444274) that displays enhanced aqueous solubility and improved selectivity ( $K_i = 16 \text{ nM}$ ,  $180 \text{ nM}$ , and  $900 \text{ nM}$  for MMP-2, -9, and -14, respectively). Minimally inhibits other MMPs ( $K_i = 3.6 \mu\text{M}$ ,  $295 \mu\text{M}$ , and  $>25 \mu\text{M}$  for MMP-3, -7, and -1, respectively). Binds to the active-site and acts as a mechanism based, irreversible inhibitor of MMPs. Further, potently suppresses cell migration and invasion of HT1080 (80% inhibition at  $2 \mu\text{M}$  and  $>25\%$  inhibition at  $100 \text{ nM}$ , respectively) and does not activate pro-MMP-2 (up to  $4 \mu\text{M}$ ) in BS-C-1 cells overexpressing MMP-14. *Purity: ≥95% by HPLC.* M.W. 399.5

**Cat. No. 444285                      500 µg                      € 117**

Ref.: Ikejiri, M., et al. 2005. *J. Biol. Chem.* 280, 33992.

### HIV-1 Protease, Human, Recombinant, *E. coli*

(Human Immunodeficiency Virus type 1, Human, Recombinant, *E. coli*)

An aspartic protease that functions as a dimer only. A key enzyme for the maturation of new infectious virions. *Purity: ≥85% by SDS-PAGE.*

**Cat. No. 382136                      10,000 U                      € 311**

Ref.: Temesgen, Z. 2001. *Expert Opin. Pharmacother.* 2, 1239; Zhang, Y.M., et al. 1997. *J. Virol.* 71, 6662; Chou, K.C., et al. 1996. *Proteins* 24, 51; Krausslich, H.G., et al. 1995. *J. Virol.* 69, 3407; Pettit, S. C., et al. 1994. *J. Virol.* 68, 8017; Navia, M.A., and McKeever, B. M. 1990. *Ann. N. Y. Acad. Sci.* 616, 73; Peng, C., et al. 1989. *J. Virol.* 63, 2550; Mervis, R. J., et al., 1988. *J. Virol.* 62, 3993.

### HCV NS3/4A Protease, Human, Recombinant, *E. coli*

(Hepatitis C Virus NS3/4A Protease, Human, Recombinant, *E. coli*)

An essential enzyme for viral replication. Responsible for cleavage at four sites within the HCV polyprotein to generate the N-terminal NS4A, NS4B, NS5A, and NS5B proteins. HCV is a positive, single-stranded RNA virus in the *Flaviviridae* family, which encodes a polyprotein precursor of about 3000 amino acids. *Purity: ≥95% by SDS-PAGE.*

**Cat. No. 444147                      10,000 U                      € 311**

Ref.: De Francesco, R., et al. 2003. *Antiviral Res.* 58, 1; Lamarre, D., et al. 2003. *Nature* 426, 186; Kolykhalov, A. et al. 2000. *J. Virol.* 74, 2046; Bartenschlager, et al. 1995. *J. Virol.* 69, 7519; Lin, C., and Rice, C. M. 1995. *Proc. Natl. Acad. Sci. U.S.A.* 92, 7622; Grakoui, A., et al. 1993. *J. Virol.* 67, 2832; Hijikata, M., et al. 1993. *Proc. Natl. Acad. Sci. U.S.A.* 90, 10773.

## **NEW** Products for Proteasome and Ubiquitination Research

### Smurf1 Ligating Enzyme, Human, Recombinant, *S. frugiperda*

Smurf1 (Smad ubiquitination regulatory factor 1) is Smad specific ubiquitin E3 ligase 1, that interacts with receptor-regulated Smads specific for the BMP pathway (Smad1 and Smad5) and triggers their ubiquitination and degradation. Smurf1 targets RhoA for degradation at cellular protrusions thus regulating cell polarity and protrusion formation. *Purity: ≥98% by SDS-PAGE.*

**Cat. No. 662078      10 µg      € 383**

Ref.: Tajima, Y., et al. 2003. *J. Biol. Chem.* **278**, 10716; Suzuki, C., et al. 2002. *J. Biol. Chem.* **277**, 39919; Ebisawa, T., et al. 2001. *J. Biol. Chem.* **276**, 12477; Zhu, H., et al. 1999. *Nature* **400**, 687; Lambris, J., et al. 1979. *J. Immunol. Methods* **27**, 55.

### Smurf2 Ligating Enzyme, Human, Recombinant, *S. frugiperda*

Smurf2 (Smad ubiquitination regulatory factor 2) is an E3 ubiquitin ligase with 83% homology to Smurf1. It selectively interacts with receptor-regulated Smads and specifically targets Smad1, Smad2, and Smad7, but not Smad4, enhances inhibitory activity of Smad7 and reduces the transcriptional activity of Smad2. Smurf1 is also involved in the ubiquitination and degradation of the TGFβ receptor and plays a critical role in its signaling. *Purity: ≥98% by SDS-PAGE.*

**Cat. No. 662079      10 µg      € 383**

Ref.: Zhang, Y., et al. 2001. *Proc. Natl. Acad. Sci. USA* **98**, 974;; Kavsak, P., et al. 2000. *Mol. Cell* **6**, 1365;; Lin, X., et al. 2000. *J. Biol. Chem.* **275**, 36818.

### UbcH8 Conjugating Enzyme, Human, Recombinant, *S. frugiperda*

A major E2-conjugating enzyme for ISG15 conjugation in reactions initiated by the ISG15-specific E1 activating enzyme. ISG15 is a ubiquitin-like protein that is conjugated to cellular proteins after IFN-α/β stimulation. UbcH8 is highly homologous to UbcH7. *Purity: ≥98% by SDS-PAGE.*

**Cat. No. 662082      100 µg      € 221**

Ref.: Kim, K.I., et al. 2004. *Mol. Cell. Biol.* **24**, 9592; Zhao, C., et al. 2004. *Proc. Natl. Acad. Sci. USA* **101**, 7578; Liu, M., et al. 2003. *J. Biol. Chem.* **278**, 1594; Tanaka, K., et al. 1998. *Mol. Cells* **8**, 503.

### UbcH9 Conjugating Enzyme, Human, Recombinant, *S. frugiperda*

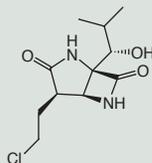
Mediates the conjugation of SUMO-1, SUMO-2, and SUMO-3 to a variety of proteins without the help of an E3 ligase. UbcH9 interacts directly with protein substrates that are modified by SUMOylation, and may help in substrate recognition. *Purity: ≥98% by SDS-PAGE.*

**Cat. No. 662083      100 µg      € 221**

Ref.: Ito, K., et al. 2001. *Eur. J. Biochem.* **268**, 2725; Ito, K., et al. 1999. *Cytogenet. Cell. Genet.* **84**, 99; Kimura, M., et al. 1997. *Cytogenet. Cell. Genet.* **78**, 107.

### Proteasome Inhibitor VIII, β-Lactam 3

A β-lactam analog of Proteasome Inhibitor VII, Antiprotealide (Cat. No. 539179) that acts as a selective and irreversible inhibitor of the 20S proteasome. Displays prolonged aqueous stability and therefore may be highly suitable for biological evaluation. *Purity: ≥95% by NMR. M.W. 260.7*



**Cat. No. 539183      100 µg      € 212**

Ref.: Hogan, P.C., et al. 2005. *J. Am. Chem. Soc.* **127**, 15386.

### Proteasome Inhibitor VII, Antiprotealide

An Omuralide-Salinosporamide hybrid that irreversibly inactivates the β5-subunit of the human 20S proteasome. Shown to be ~2.5-fold more potent than Omuralide (Cat. No. 426102) and somewhat less potent than Salinosporamide A. *Purity: ≥95% by NMR. M.W. 275.7*

**Cat. No. 539179      50 µg      € 158**

Ref.: Reddy, L.R., et al. 2005. *J. Am. Chem. Soc.* **127**, 8974.

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E-mail [techservice@merckbiosciences.co.uk](mailto:techservice@merckbiosciences.co.uk)

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