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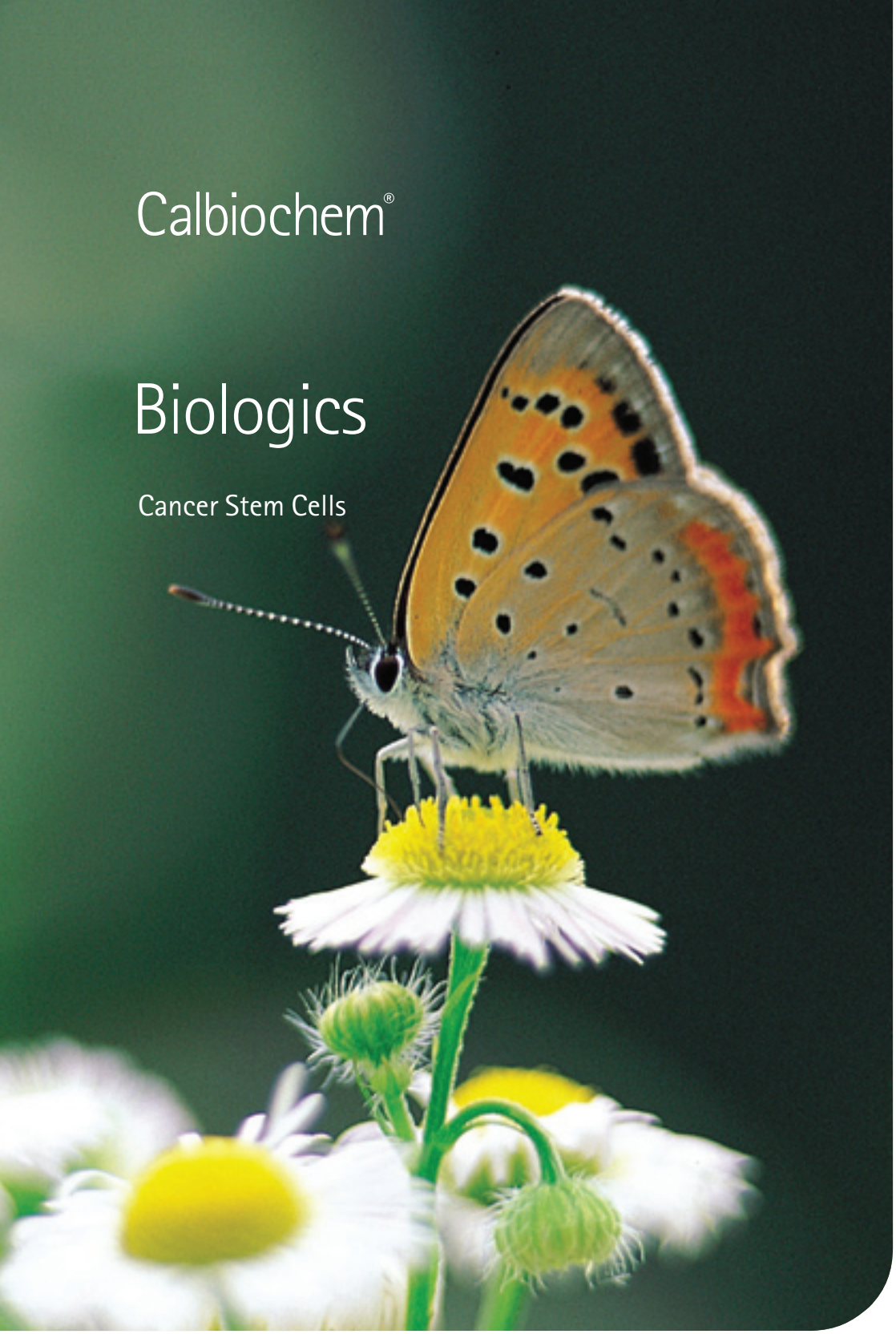
Biologics

Cancer Stem Cells



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Cancer Stem Cells:

The Real Perpetrators in Cancer Growth and Progression

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Stem cells, unspecified precursor cells, have the unique ability to self-renew and generate additional stem cells as well as to differentiate into various progenitor cells in response to appropriate signals. These functional properties have led researchers to explore opportunities for developing new strategies for tissue repair, replacement, and regeneration. Stem cells are classified as either embryonic stem cells (ES) or adult stem cells. ES are derived from the inner cell mass of preimplantation embryos and are considered to be the most pluripotent. They can undergo infinite, undifferentiated proliferation *in vitro* and can also differentiate into a wide variety of somatic and extra-embryonic tissues. Adult stem cells are unspecialized cells found in differentiated tissues that can self-renew and differentiate into mature cell types of the specific tissue. In contrast to ES, adult stem cells can proliferate only for a limited number of cycles and their response to differentiation signals declines with each cycle.

Both normal stem cells and cancer cells possess the ability to self-renew and many pathways that are classically associated with cancer are also involved in the regulation of normal stem cell development. For example, blocking of apoptosis by enforced expression of Bcl-2 can result in increased numbers of hematopoietic stem cells (HSCs). Signaling pathways associated with oncogenesis, such as the Notch, Sonic hedgehog (Shh), and Wnt pathways are also involved in the regulation of self-renewal of stem cells. Notch activation in HSCs by Jagged-1 increases the amount of primitive progenitor activity, suggesting that Notch activation promotes HSC self-renewal and the maintenance of their multipotentiality.

Shh, a secreted morphogen, has been implicated in several embryonic developmental processes. It displays inductive, proliferative, neurotrophic, and neuroprotective properties. Human HSCs exhibit increased self-renewal in response to Shh stimulation *in vitro*, albeit in combination with other growth factors. Shh signaling is required throughout embryonic development and is involved in the determination of cell fate and embryonic patterning during early vertebrate development. Shh also functions with other signaling molecules, such as the fibroblast growth factors and bone morphogenetic proteins, to mediate developmental processes. Mutations in any of the components of the Shh pathway can lead to congenital defects and diseases, including cancer. Hence, the Shh pathway has become a potential target for drug development for the treatment of cancers and degenerative diseases.

Shh often works in concert with the Wnt signaling protein to set embryonic development patterns. Wnt proteins are intercellular signalling molecules that regulate development in several organisms and contribute to cancer when dysregulated. The Wnt pathway uses β-catenin to transduce its signals to the nucleus. The expression of Wnt proteins in the bone marrow indicates that they may have some regulatory influence on HSCs. Using highly purified mouse bone-marrow HSCs, Reya et al. (2001) have shown that overexpression of activated β-catenin in long-term cultures of HSCs expands the pool of transplantable HSCs. In additon, over-expression of axin, an inhibitor of Wnt signaling pathway, leads to inhibition of HSC proliferation and increased death of HSCs *in vitro*. Higher levels of β-catenin are also reported to increase the proliferative capacity of cultured human keratinocytes suggesting that Wnt signaling promotes stem cell self-renewal.

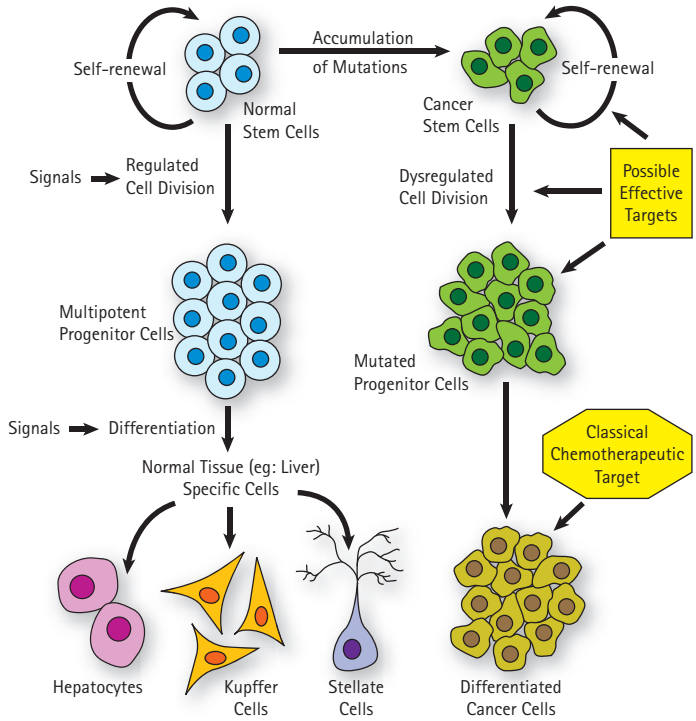
In spite of their tremendous capacity for self-renewal, normal stem cells are generally quiescent and remain in the G_0 stage. Due to the fact that stem cells can repair their DNA as they self-renew, they have the potential to accumulate more mutations, some of which may transform them into cancer stem cells. These cancer stem cells may be the ones that survive various bouts of chemotherapy. Also, any abnormality in the signaling processes during stem cell differentiation can lead to tumorigenesis. Cancer stem cells often renew themselves in a poorly regulated manner in contrast to normal stem cells, which are strictly regulated for self-renewal.

It is believed that stem cells are often the target of genetic events that are necessary for malignant transformation. Cancer researchers have concentrated on identifying the genetic alterations that transform cells into a cancer phenotype. If one views a tumor as an abnormal organ, then the principles of normal stem cell biology can be

applied to better understand how tumors develop. Both normal stem cells and tumorigenic cells have extensive proliferative potential with the ability to give rise to new, normal or abnormal tissues. Because most tumors have a clonal origin, tumorigenic cancer cells must give rise to phenotypically diverse cell types, including cancer cells with indefinite proliferative potential and those with limited or no proliferative potential. Hence, tumorigenic cancer cells undergo processes that are analogous to the self-renewal and differentiation of normal stem cells.

The role of stem cells in normal tissue turnover is barely understood, and even less is known about the role of stem cells in tumor growth and progression. A tumor mass can be considered as an abnormal organ that contains a variety of tumor cells, which are at different stages of differentiation. It is believed that in this "abnormal organ" only a limited number of cells possess the capacity to self-renew. For example, it has been shown that in leukemia and multiple myeloma only a small subset of cancer cells can lead to extensive proliferation. Park et al. (1971) showed that when mouse myeloma cells obtained from mouse ascites are separated from normal hematopoietic cells and are placed in clonal *in vitro* colony-forming assays, only 1 in 10,000 cancer cells go to form colonies. Also, when leukemic cells are transplanted *in vivo*, less than 4% of cells are able to form spleen colonies. These clonogenic leukemic cells can be described as leukemic stem cells. Bonnet and Dick (1997) demonstrated that human acute myeloid leukemia (AML) stem cells could be identified and purified as $CD34^+/CD38^-$ cells. Although, these cells represent only a very small proportion of AML cells they were the only cells capable of transferring AML from human patients to NOD/SCID mice. Several other studies have shown that in solid tumors cells are phenotypically heterogeneous and only a small proportion of these cells are clonogenic in culture and *in vivo*. These studies indicate that only a small number of cancer cells are actually tumorigenic and can be considered as cancer stem cells.

Identification and selective destruction of cancer stem cells would certainly change the way cancer therapy is implemented. Currently, all phenotypically diverse cancer cells are treated in a manner that considers each cell to have unlimited proliferative and metastatic potential. One must note here that either a highly effective immune surveillance system in our body kills most cancer cells before they have any opportunity to form a tumor or most cancer cells are devoid of capability to form a new tumor. If the latter is truly the case, the appropriate therapy will be able to identify and destroy cancer stem cells before they proliferate and differentitate into different cancer phenotypes. Evaluation



of success rates of most existing therapies is based on their ability to shrink solid tumors. However, they fail to eradicate solid tumors completely and any shrinkage is only transient. There exists a strong possibility that cancer stem cells are more resistant to chemotherapeutic agents than other tumor cells with "limited" proliferative potential. Chemotherapeutic agents may cause complete regression of tumors, but might spare enough cancer stem cells to allow regrowth.

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NEW Bone Morphogenetic Proteins

Bone morphogenetic proteins (BMPs) are a group of developmental regulatory factors of the transforming growth factor-β superfamily. They are produced by osteoblasts and other bone cells and affect osteoblast proliferation and differentiation. BMPs are resident in the extracellular matrix and their signaling is controlled by binding to matrix proteins. 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. Aberrant regulation of BMPs is an important factor in cancer and various connective-tissue diseases.

Name	Cat. No.	Comments	Size	Price
BMP-2, Human, Recombinant, *E. coli*	203641	A disulfide-bonded homodimeric protein that plays an important role in cardiac morphogenesis.	2 µg	€ 116
BMP-4, Human, Recombinant, *E. coli*	203642	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.	2 µg	€ 116
BMP-6, Human, Recombinant, *E. coli*	203643	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.	2 µg	€ 116
BMP-6, Human, Recombinant, Mouse	203644	Strongly induces phosphorylation and nuclear accumulation of Smad5. BMPs have also been shown to be involved in embryogenesis and morphogenesis of cells of osteoblastic lineage. A positive regulator of keratinocyte differentiation.	20 µg	€ 593
BMP-7, Human, Recombinant, Mouse	203645	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.	2 µg	€ 116
BMP Receptor IB/Fc Chimera, His•Tag®, Human, Recombinant, Mouse	203648	The extracellular domain of human BMPR-IB (Lys^{14}-Arg^{126}) attached to a signal peptide sequence from CD33, was fused to the carboxy-terminal 6X His•Tag® Fc region of human IgG_1 via a polypeptide linker. The recombinant receptor chimera is expressed as a soluble disulfide-linked homodimer with serine/threonine kinase activity.	100 µg	€ 520

Inducers and Blockers of Stem Cell Differentiation

Name	Cat. No.	Comments	Size	Price
Cardiogenol C	217460	A cell-permeable, potent inducer of differentiation of embryonic stem cells into cardiomyocytes (EC_{50} = 100 nM).	5 mg	€ 173
Cyclopamine, *V. californicum*	239803	A natural alkaloid isolated that acts as a specific Sonic hedgehog signaling (Shh) antagonist. Blocks the proliferation of adult forebrain subventricular zone stem cells.	1 mg	€ 148
Cyclopamine-KAAD	239804	A potent analog of Cyclopamine (Cat. No. 239803) that specifically inhibits the Hedgehog (Hh) signaling with similar or lower toxicity (IC_{50} = 20 nM in Shh-LIGHT2 assay). Suppresses both the ShhNp-induced pathway activity and SmoA1-induced reporter activity.	100 µg	€ 158
GSK-3 Inhibitor IX (BIO)	361550	A cell-permeable, highly potent, selective, reversible, and ATP-competitive inhibitor of GSK-3α/β (IC_{50} = 5 nM). Inhibition of GSK by BIO results in the activation of Wnt-signaling pathway and sustained pluripotency in human and murine embryonic stem cells. Also induces the differentiation of neonatal cardiomyocytes.	1 mg	€ 115
Jervine	420210	A cell-permeable steroidal alkaloid similar to Cyclopamine (Cat. No. 239803) that blocks Sonic Hedgehog signaling (IC_{50} ~ 500-700 nM in s12 cells).	1 mg	€ 93
Purmorphamine	540220	A cell-permeable inducer of osteoblast differentiation of multipotent mesenchymal progenitor cells C3H10T1/2 (EC_{50} = 1 µM) and lineage-committed preosteoblasts MC3T3-E1.	5 mg	€ 173
Reversine	554717	A cell-permeable dedifferentiation-inducing agent that induces mouse C2C12 myoblast cells to become multipotent mesenchymal progenitor cells.	5 mg	€ 173
SANT-1	559303	A potent blocker of the Sonic hedgehog signaling (IC_{50} = 20 nM in the Shh-LIGHT2 assay). Acts by binding directly to Smoothened (Smo; K_d ~ 1.2 nM). Blocks the inductive action of WntA3 and reduces differentiation of embryonic stem cells into neuronal cells.	5 mg	€ 130
Stem Cell Proliferation Inhibitor	569620	A tetrapeptide (Ac-SDKP) that acts as a natural inhibitor of pluripotent hematopoietic stem cell proliferation. Protects bone marrow against chemotherapeutic agents, ionizing radiations, hyperthermia, or phototherapy-induced toxicity.	5 mg	€ 159
Stem Cell Factor, Human, Recombinant, *E. coli*	569600	A hematopoietic growth factor that stimulates the growth of cells of multiple lineage. Binds to c-Kit and mediates survival, growth, and function of hematopoietic progenitor cells and mast cells.	10 µg	€ 376

Statins and Stem Cell Differentiation

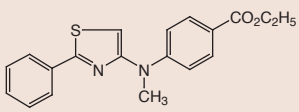
HMG-CoA reductase inhibitors (statins) have been shown to reduce mortality and cardiovascular morbidity in patients with hyperlipidemia and those with coronary artery disease. Stem cell plasticity that involves mobilization of stem cells from the bone marrow and other niches, homing to the area of tissue injury and transdifferentiation into functional cardiomyocytes is an important mechanism of reducing the effects of cardiac tissue injury. Statins are reported to stimulate bone formation *in vitro* and in rodents by increasing the expression of bone morphogenetic protein-2 (BMP-2), thus indicating a new therapeutic role in the treatment of osteoporosis.

Name	Cat. No.	Comments	Size	Price
Fluvastatin, Sodium Salt	344095	A synthetic HMG-CoA reductase inhibitor (IC_{50} = 40–100 nM) that suppresses the growth of human mesenchymal stem cells. Also shown to reduce proliferation of NRK-49F cells in a dose-dependent manner.	25 mg	€ 210
Lovastatin	438185	An HMG-CoA reductase inhibitor that restores impaired remyelination mediated through enhanced survival and differentiation of oligodendrocyte progenitors in the spinal cord of treated experimental autoimmune encephalomyelitis animals. Also reported to suppress the growth of human mesenchymal stem cells	25 mg	€ 115
Lovastatin, Sodium Salt	438186	The carboxylate form of Lovastatin (Cat. No. 438185) that is active in whole cells and cell-free assays.	5 mg	€ 164
Mevastatin	474700	A potent inhibitor of HMG-CoA reductase that inhibits myoblast fusion. Also may induce bone morphogenic protein-2 (BMP-2). Causes a 3-fold increase in the expression of the telomere capping protein TRF2. Reported to block the senescence of endothelial progenitor cells in culture.	50 mg	€ 98
Mevastatin, Sodium Salt	474705	The carboxylate form of Mevastatin (Cat. No. 474700) that is active in whole cells and in cell-free assays.	5 mg	€ 112
Pravastatin, Sodium Salt	524403	A competitive inhibitor of HMG-CoA reductase that improves cardiac function after myocardial infarction. Shown to inhibit both erythroid and granulocyte-macrophage colony formation by total or CD34-positive bone marrow cells	25 mg	€ 91
Simvastatin	567020	An inhibitor of HMG-CoA reductase that blocks proliferation of human smooth muscle cells. Shown to protect the cardiac myocyte progenitor cells against the cytotoxicity of cytokine-induced nitric oxide production.	50 mg	€ 203
Simvastatin, Sodium Salt	567021	The carboxylate form of Simvastatin (Cat. No. 567020) that is active in whole cells and in cell-free preparations.	5 mg	€ 164

Neuropathiazol

(KHS2)

A cell-permeable thiazole compound that acts as a potent and selective inducer of neuronal differentiation. Shown to induce the differentiation of adult neural progenitor HCN cells into mature neurons (10 µM for 10 days). Competitively suppresses astrogliogenesis by LIF/BMP2/FBS in a dose-dependent manner. *Purity: ≥96% by HPLC.* M.W. 338.4



Cat. No. 480745 **5 mg** **€ 132**

"Honestly, I didn't realize I was filtering that fast!"

Selected Antibodies for Stem Cell Research

Name	Cat. No.	Comments	Size	Price
Anti-CD106 Mouse mAb (1.G11B1)	217635	Liquid, protein A purified. Immunogen used was human endothelial cells. Recognizes CD106 (VCAM-1). Reacts with human. **FC, FS, IP**	100 µg	€ 262
Anti-CD34 Mouse mAb (QBEnd/10)	OP164	Liquid, protein G purified. Immunogen used was detergent-solubilized vesicular suspension prepared from a perfusate of human term placenta. Recognizes CD34 selectively expressed on human lymphoid and myeloid hematopoietic progenitor cells and on vascular endothelial cells in normal tissues and benign and malignant proliferations. Reacts with human. **PS, FC**	100 µg	€ 294
Anti-Nestin Mouse mAb (2C13B9)	ST1111	Liquid, purified. Immunogen used was a GST fusion protein containing amino acids 1464-1614 of human nestin. Recognizes the ~220-240 kDa Nestin protein in U251 cells. Reacts with human. **FS, IB, IC**	100 µl	€ 218
Anti-CD44 Rat mAb (A020)	217594	Liquid, purified by ammonium sulfate precipitation and DEAE chromatography. Immunogen used was purified human lymphocyte CD44. Recognizes the ~85-95 kDa CD44 protein (gp90 in human and gp85 or Pgp-1 in mouse). Reacts with bovine, canine, human, mouse, porcine, rabbit. **ELISA, FC, IB, IF, IH, IP, RIA**	100 µl	€ 328
Anti-CD29 Mouse mAb (4B7R)	217648	Liquid, protein A purified. Immunogen used was human ocular melanoma cell line, V+B2. Recognizes the CD29 β1 integrin subunit in Nalm-6 cells. Reacts with human. **FC, FS, IP, PS**	100 µg	€ 273
Anti-CD4 Mouse mAb (QS4120)	217575	Liquid, purified. Immunogen used was $CD4^+$ transfectant/human CEM. Reacts with human. **2D PAGE, ELISA, FC, FS**	100 µg	€ 172
Anti-CD10 Mouse mAb (SN5c)	OP161	Liquid, protein G purified. Immunogen used was a membrane preparation of human B-lineage leukemia cells. Recognizes the ~100 kDa CD10 protein. Reacts with human. **FC, FS, IP,**	100 µg	€ 294
Anti-PCOLE-1 Rabbit pAb	208769	Liquid, immunoaffinity purified. Immunogen used was a synthetic peptide corresponding to amino acids at the end of the CUB-2 domain and beginning of the linker region of human PCOLE-1. Recognizes the mature ~50-55 kDa PCOLE-1 protein and the ~34 and ~36 kDa proteolytic fragments of PCOLE-1. Reacts with human, mouse, porcine. **IB**	100 µg	€ 329
Anti-PCOLE-2 Rabbit pAb	208770	Liquid, immunoaffinity purified. Immunogen used was a synthetic peptide corresponding to amino acids at the end of the CUB-2 domain and beginning of the linker region of human PCOLE-2. Recognizes the mature ~50-55 kDa PCOLE-2 protein and the ~34 and ~36 kDa proteolytic fragments of PCOLE-2. Reacts with human, mouse, porcine. **IB**	100 µg	€ 334
Anti-BNF1 (150-250) Rabbit pAb	CA1021	Liquid, immunoaffinity purified. Immunogen used was a synthetic peptide corresponding to amino acids within residues 150-250 of human BNF1. Detects the ~50 kDa BNF1 protein that can act as a BMP antagonist. Reacts with human. **IB**	50 µg	€ 153

ELISA: enzyme-linked immunosorbent assay; **FC**: flow cytometry; **FS**: frozen sections; **IB**: immunoblotting; **IC**: immunocytochemistry; **IP**: immunoprecipitation; **IP**: immunoprecipitation; **NT:** neutralization; **PS**: paraffin sections; **RIA**: radioimmunoassay

NEW Protein Kinases for your Signal Transduction Research

Akt2, GST-Fusion Protein, Active, Human, Recombinant,

(PKBβ, GST-Fusion Protein, Active, Human, Recombinant)

Human, recombinant Akt2 (amino acids 1-119 minus the PH domain) expressed as a GST-fusion protein using a baculovirus expression system. The recombinant protein is also expressed with S473D and T308E mutations. Akt2 is activated in response to various growth factors and is known to phosphorylate a number of downstream proteins. *Specific activity: ≥ 45 units/mg protein. Purity: ≥80% by SDS-PAGE*

Cat. No. 124021 **20 µg** **€ 282**

Ref.: Baer, K., et al. 2005. *Biochim. Biophys. Acta.* **1725,** 340.

Akt3, GST-Fusion Protein, Active, Human, Recombinant, *S. frugiperda*

(PKB_γ; Protein Kinase B_γ, GST-Fusion Protein, Human, Recombinant)

Full-length, human, recombinant Akt3 fused to GST at the N-terminus and expressed Sf9 cells using a baculovirus expression system. Akt3 plays an important role in cellular metabolism, apoptosis and proliferation. *Specific activity: ≥ 176 nmol/min/mg protein. Purity: ≥92% by SDS-PAGE*

Cat. No. 124022 **5 µg** **€ 93**

Ref.: Nicholson, K.M., et al. 2002. *Cell. Signal.* **14,** 381; Okano, J., et al. 2000. *J. Biol. Chem.* **275,** 30934.

NEW Protein Kinases for your Signal Transduction Research *(continued...)*

Aurora A, His•Tag®and S•Tag™, Human Recombinant, *S. frugiperda*

Human full-length Aurora A (amino acids 1-403) expressed in *Spodoptera frugiperda* insect cells with N-terminal His•Tag® and S•Tag™ sequences. Plays an important role in chromosome segregation and cell division. *Specific activity: >500 units/mg protein. Purity: ≥80% by SDS-PAGE.*

Cat. No. 481410 **10 µg** **€ 278**

Ref.: Lennon, G., et al. 1996. *Genomics* **33,** 151.

MAPKAP Kinase 2, GST-Fusion Protein, Active, Human, Recombinant, *S. frugiperda*

Human, recombinant MAPKAPK 2 fused to GST at the N-terminus and expressed in Sf9 cells using a baculovirus expression system. MAPKAPK2 plays a key role in stress and inflammatory responses, nuclear export, and cell proliferation. *Specific activity: ≥216 nmol/min/mg protein. Purity: ≥90% by SDS-PAGE.*

Cat. No. 475861 **5 µg** **€ 139**

Ref.: McCormick, C., et al. 2005. *Science* **307,** 739; Maizels, E.T., et al. 2001. *Molec. Endocr.* **15,** 716; Stokoe, D., et al 1993. *Biochem. J.* **296,** 843.

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

Full-length, human, recombinant PKCι expressed with an N-terminal GST-fusion protein. Plays an important role in neuronal apoptosis and degeneration in Alzheimer's disease. *Specific activity: ≥565 nmol/min/mg protein. Purity: ≥90% by SDS-PAGE.*

Cat. No. 539685 **5 µg** **€ 89**

Ref.: Gustrafson, W.C., et al. 2004. *J. Biol. Chem.* **279,** 9400; Zhang, J., et al. 2004. *J. Biol. Chem.* **279,** 22118.

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

Full-length, human, recombinant PKCμ fused to GST at the N-terminus. A Ca^{2+}-independent, phospholipid-dependent isoform of PKC. *Specific activity: ≥560 nmol/min/mg protein. Purity: ≥90% by SDS-PAGE*

Cat. No. 539686 **5 µg** **€ 93**

Ref.: Hausser, A., et al. 2001. *FEBS Lett.* **492,** 39; Hausser, A., et al. 1999. *J. Biol. Chem.* **274,** 9258; Nishikawa, K., et al. 1998. *J. Biol. Chem.* **273,** 23126; Rennecke, J., et al. 1996. *Eur. J. Biochem.* **242,** 428; Sidorenko, S.P., et al. 1996. *Immunity* **5,** 353; Johannes, F.J., et al. 1994. *J. Biol. Chem.* **269,** 6140.

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

Full-length, human, recombinant PKCν expressed with an N-terminal GST-fusion protein. Plays an important role in cell differentiation and proliferation. *Specific activity: ≥67 nmol/min/mg protein. Purity: ≥80% by SDS-PAGE.*

Cat. No. 539687 **5 µg** **€ 93**

Ref.: Matthews, S.A., et al. 2003. *J. Biol. Chem.* **278,** 9086; Rey, O., et al. 2003. *J. Biol. Chem.* **278,** 23773; Hayashi, A., et al. 1999. *Biochim. Biophys. Acta* **1450,** 99.

Protein Kinase A, Catalytic Subunit, Bovine Heart

Catalytic subunit purified from bovine heart. Phosphorylates target proteins at the Arg-Arg-x-Ser-x recognition motif. Does not require cAMP for activation. *Specific activity: ≥20,000 units/µg protein. Purity: ≥95% by SDS-PAGE.*

Cat. No. 539576 **25 µg** **€ 260**

Ref.: Corbin, J.D., et al. 1988. *Methods Enzymol* **159,** 74; Rannels, S.R., et al 1983. *Methods Enzymol.* **99,** 55; Witt, J.J. and Roskoski, R. Jr. 1975. *Anal Biochem.* **66,** 253.

Protein Kinase A, Regulatory Subunit Type II, Bovine Heart

Regulatory subunit of PKA purified from bovine heart. The physical association of catalytic subunit with the regulatory subunit blocks the catalytic activity in the cytoplasm and inhibits the movement of C subunit into the nucleus. *Specific activity: ≥1000 units/µg protein. Purity: ≥95% by SDS-PAGE.*

Cat. No. 539577 **50 µg** **€ 167**

Ref.: Corbin, J.D., et al. 1988. *Methods Enzymol* **159,** 74; Rannels, S.R., et al 1983. *Methods Enzymol* **99,** 55; Witt, J.J. and Roskoski, R. Jr. 1975. *Anal Biochem.* **66,** 253.

Protein Kinase G, Iα, Bovine Lung

Catalytic subunit of PKG involved in the regulation of smooth muscle relaxation, platelet function, and cell division. Unlike PKA, its activation does not involve physical dissociation from regulatory domains. The activated enzyme phosphorylates target proteins within recognition motif Arg-Lys-Arg-Ser-Arg-Ala-Glu *Specific activity: ≥1300 units/µg protein. Purity: ≥95% by SDS-PAGE.*

Cat. No. 539578 **4 µg** **€ 222**

Ref.: Brophy, M.C., et al. 2006. *J. Vasc. Res.* **39,** 95; Colbran J.L., et al. 1992. *J. Biol. Chem.* **267,** 9589; Corbin, J.D. and Doskeland, S.O. 1983. *J Biol Chem* **258,** 11391.

Raf1, GST-Fusion Protein, Active, Human, Recombinant, *S. frugiperda*

Human, recombinant Raf1 consisting of amino acids 307-648 fused to GST at the N-terminus. *Specific activity: ≥ 90 nmol/min/mg protein. Purity: ≥90% by SDS-PAGE.*

Cat. No. 553012 **5 µg** **€ 139**

Ref.: O'Neill, E., et al. 2004. *Science* **306,** 2267; Alavi, A., et al. 2003. *Science* **301,** 94; Lorenz, K., et al. 2003. *Nature* **426,** 574; Wang, H.G., et al. 1996. *Cell* **87,** 629; Li, P., et al. 1991. *Cell* **64,** 479; Rapp, U.R., et al. 1983. *Proc. Natl. Acad. Sci. USA* **80,** 4218.

SGK1, GST-Fusion Protein, Active, Human, Recombinant, *S. frugiperda*

(Serum/glucocorticoid regulated kinase 1, GST-Fusion Protein, Human, Recombinant)

Human, recombinant SGK1 consisting of amino acids 61-431 expressed with an N-terminal GST-fusion protein. A member of the AGC family, regulated by growth factors and stress-mediated signaling. It is involved in the regulation of epithelial Na^+ channels. *Specific activity: ≥55 nmol/min/mg protein. Purity: ≥95% by SDS-PAGE.*

Cat. No. 535851 **5 µg** **€ 93**

Ref.: Busjahn, A., et al. 2002. *Hypertension* **40,** 256; Brunet, A., et al. 2001. *Mol. Cell. Biol.* **21,** 952; Kobayashi, T., et al. 1999. *Biochem. J.* **344,** 189; Shelly, C., and Herrera, R. 2002. *J. Cell Sci.* **115,** 1985.

Src1, GST-Fusion Protein, Active, Human, Recombinant, *S. frugiperda*

Full-length, human, recombinant Src1 expressed with an N-terminal GST-fusion protein. Regulates cell proliferation, differentiation, motility, and adhesion. *Specific activity: ≥ 98 nmol/min/mg protein. Purity: ≥90% by SDS-PAGE.*

Cat. No. 539688 **5 µg** **€ 93**

Ref.: Onate, S. A., et al. 1995. *Science* **270,** 1354.

ZAP70, GST-Fusion Protein, Active, Human, Recombinant, *S. frugiperda*

Full-length, human, recombinant ZAP70 protein expressed with an N-terminal GST-fusion protein. The ζ-chain T-Cell receptor associated protein Tyrosine Kinase. Regulates responses to T-cell receptor activiation. *Specific activity: ≥ 96 nmol/min/mg protein. Purity: ≥90% by SDS-PAGE.*

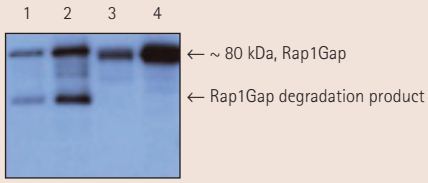
Cat. No. 539689 **5 µg** **€ 93**

Ref.: Paz, P.E., et al. 2001. *Biochem. J.* **356,** 461; Skov, S., et al. 1997. *J. Immunol.* **158,** 3189; Nel, A. E., et al. 1995. *J. Biol. Chem.* **270,** 18428.

Anti-Rap1Gap Rabbit pAb

Liquid, purified. Immunogen used was a full length recombinant human Rap1Gap containing a His•Tag® sequence. Recognizes the ~80 kDa Rap1Gap protein in bovine brain (high speed supernatant) and INS-1 (832/13) cells expressing recombinant Rap1Gap protein. Reacts with human, mouse, rat. Suitable for immunoblotting and immunoprecipitation.

Cat. No. ST1112 **100 µl** **€ 246**



Detection of Rap1Gap by immunoblotting. Sample: Purified recombinant Rap1Gap (2 ng, lane 1; 5 ng, lane 2). Whole cell lysates from Ins1 (832/13) cells expressing Rap1Gap (lane 3), and bovine brain high speed supernatant (25 µg) (lane 4). Primary antibody: Anti-Rap1Gap Rabbit pAb (Cat. No. ST1112) (1:1000). Detection: chemiluminescence.

14-3-3β, GST-Fusion, Human, Recombinant, *E. coli*

Recombinant, human 14-3-3β, fused to GST at the N-terminus with a thrombin cleavage site and expressed in *E. coli*. Useful for protein-protein interaction assays and gel overlays. 14-3-3β plays an important role in the proliferation and oncogenic transformation of NIH/3T3 cells through enhancement of Raf-1 activation and resultant augmentation of signaling in the MAPK cascade. *Purity: ≥90% by SDS-PAGE.*

Cat. No. 100071 **100 µg** **€ 306**

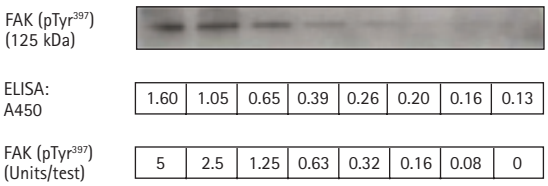
Ref.: Ellis, J.J., et al. 2002. *Mol. Cell. Biol.* **22,** 6809; Yaffe, M.B., et al. 2002. *FEBS Lett.* **513,** 53; Grozinger, C.M. and Schreiber, S.L. 2000. *Proc. Natl. Acad. Sci. USA* **97,** 7835; Takihara, Y., et al. 2000. *Carcinogenesis* **21,** 2073; Furlantetto, R.W., et al. 1997. *Biochem. J.* **327,** 765.

NEW Assay Kits to Detect Phosphorylation States of Proteins

PhosphoDetect™ FAK (pTyr^{397}) ELISA Kit

Format: 96-well plate
Sensitivity: <0.9 unit/ml
Assay range: 1.6-100 units/ml
A solid phase sandwich ELISA for detection and quantitation of focal adhesion kinase phosphorylated at Tyr^{397}. Suitable for use with human, mouse, and rat samples.

Cat. No. CBA062 **1 kit** **€ 534**



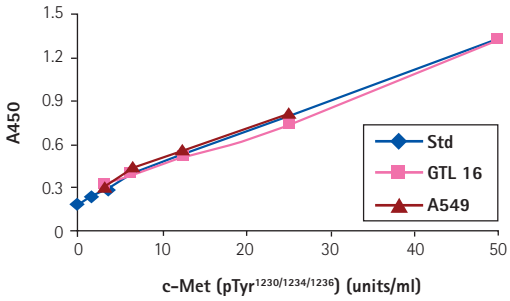
ELISA: A450	1.60	1.05	0.65	0.39	0.26	0.20	0.16	0.13
FAK (pTyr^{397}) (Units/test)	5	2.5	1.25	0.63	0.32	0.16	0.08	0

Sample: 3T3L1 cells stimulated with sodium orthovanadate. The sensitivity of this ELISA was compared to immunoblotting using known quantities of FAK (pTyr^{397}). The data show the greater sensitivity of the ELISA method. The bands shown in the immunoblot data were developed using anti-FAK (pTyr^{397}). Detection: chemiluminescent.

PhosphoDetect™ c-Met (pTyr$^{1230/1234/1235}$) ELISA Kit

Format: 96-well plate
Sensitivity: <0.25 unit/ml
Assay range: 1.56-100 units/ml
A solid phase sandwich ELISA for detection and quantitation of c-Met. Phosphorylated at Tyr$^{1230/1234/1235}$. Suitable for use with human samples.

Cat. No. CBA073 **1 kit** **€ 534**

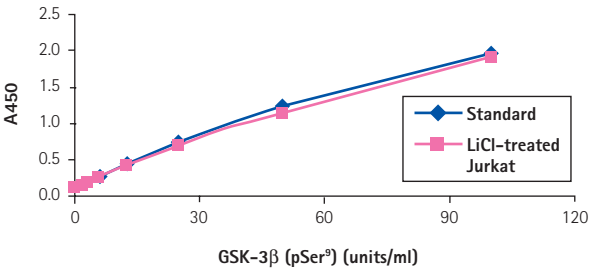


Lysates of sodium orthovanadate treated GTL16 and A549 cells were serially diluted in standard diluent buffer and natural c-Met (pTyr$^{1230/1234/1235}$) levels were measured. The absorbance was plotted against c-Met (pTyr$^{1230/1234/1235}$) standard curve.

PhosphoDetect™ GSK-3β (pSer^{9}) ELISA Kit

Format: 96-well plate
Sensitivity: <0.4 unit/ml
Assay range: 1.6-100 units/ml
A solid phase sandwich ELISA for detection and quantitation of GSK-3β. Phosphorylated at Ser^{9}. Suitable for use with human, mouse, and rat samples.

Cat. No. CBA069 **1 kit** **€ 534**

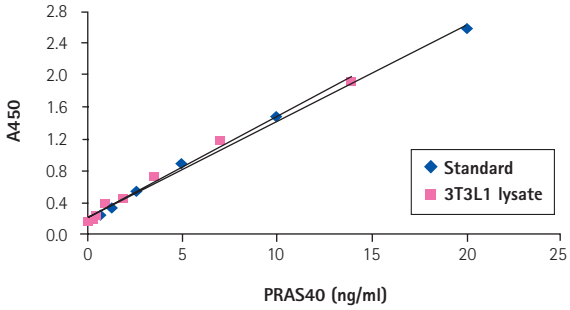


Lithium chloride treated Jurkat cells were lysed and the lysates were serially diluted in standard diluent buffer. The absorbance was plotted against the GSK-3β (Ser^{9}) standard curve.

PRAS40 ELISA Kit

Format: 96-well plate
Sensitivity: <200 pg/ml
Assay range: 0.313-20 ng/ml
A solid phase sandwich ELISA for detection and quantitation of PRAS40 (Proline-Rich Akt substrate of 40 kDa). The detection monoclonal antibody detects PRAS40 regardless of its phosphorylation state. PRAS40 is a 14-3-3 binding protein that is a direct substrate of Akt. Suitable for use with human, mouse, and rat samples.

Cat. No. CBA066 **1 kit** **€ 534**



3T3L1 cell lysates were serially diluted in standard diluent buffer and levels of natural PRAS40 were measured. The absorbance of each dilution was plotted against the PRAS40 standard curve.

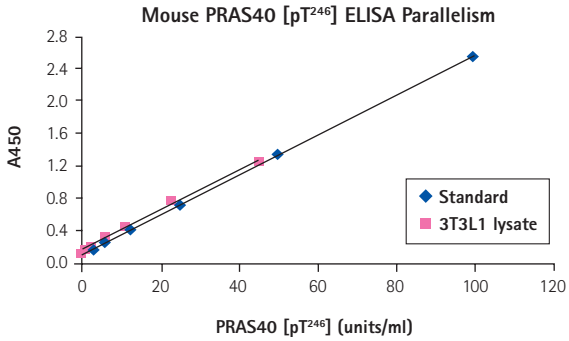
Technical Support Freephone 0800 100 3496
E-mail techservice@merckbiosciences.de
Visit our website www.merckbiosciences.de

NEW Assay Kits *(continued...)*

PhosphoDetect™ PRAS40 (pThr^{246}) ELISA Kit

Format: 96-well plate
Sensitivity: <0.5 unit/ml
Assay range: 1.6–100 units/ml
A solid phase sandwich ELISA for detection and quantitation of PRAS40 phosphorylated at Thr^{246}. PRAS40 is a 14-3-3 binding protein that is a direct substrate of Akt. Suitable for use with human, mouse, and rat samples.

Cat. No. CBA067 **1 kit** **€ 534**



3T3L1 cells grown at 37°C in DMEM containing 10% fetal bovine serum were lysed in cell lysis buffer. Lysate was diluted in standard diluent buffer over the range of the assay and measured for PRAS40 (pThr^{246}).

Cholesterol/Cholesteryl Ester Quantitation Kit

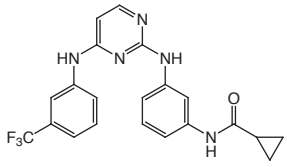
Format: 96-well plate
Sample type: Cells, tissues, serum
A sensitive colorimetric or fluorometric assay for the quantitative measurement of cholesterol, cholesteryl ester, or both. Measurement by spectrophotometry at 570 nm or fluorometry at Ex/Em = 535/587 nm. This assay kit can measure cholesterol and total cholesterol (cholesterol + cholesterol ester) by adding cholesterol esterase to the reaction, or only cholesteryl ester by subtracting the value of cholesterol from the total value of cholesterol plus cholesteryl esters. The fluorometric assay can detect 0.02-1 µg/well and is 4-10 fold more sensitive than colorimetric assay. Each kit is suitable for up to 100 assays.

Cat. No. 428901 **1 kit** **€ 302**

NEW Protein Kinase Inhibitors for your Cell Signaling Research

Aurora Kinase Inhibitor III

[Cyclopropanecarboxylic acid-(3-(4-(3-trifluoromethyl-phenylamino)-pyrimidin-2-ylamino)-phenyl)-amide]
A cell-permeable, ATP-competitive, and potent, but non-selective inhibitor of Aurora A (IC_{50} = 42 nM). At higher concentrations, also inhibits the activities of other kinases, such as Lck, Bmx, IGF-1R, and Syk (IC_{50} = 131, 386, 591, and 887 nM, respectively). *Purity: ≥98% by HPLC.* M.W. 413.4

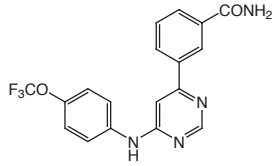


Cat. No. 189405 **1 mg** **€ 79**

Ref.: Zhang, Q., et al. 2006. *J. Am. Chem. Soc.* **128,** 2182.

Bcr-abl Inhibitor

[GNF-2; (3-(6)-(4-Trifluoromethoxy-phenylamino)-pyrimidin-4-yl)-benzamide]
A cell-permeable pyrimidine compound that binds to the c-abl myristoyl binding pocket and acts as an allosteric, non-ATP-competitive inhibitor of Bcr-abl activity and Bcr-abl-dependent cellular functions. Blocks proliferation of Bcr-abl expressing cells (IC_{50} = 138 nM, 194 nM, 268 nM and 273 nM in Ba/F3.p210, Ba/F3.p^{185Y253H}, SUP-B15 and Ba/F3.p^{210E255V}, and K562, respectively). *Purity: ≥97% by HPLC.* M.W. 374.3



Cat. No. 197221 **5 mg** **€ 121**

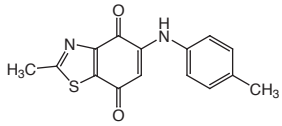
Ref.: Adrian, F.J., et al. 2006. *Nat. Chem. Biol.* **2,** 95.

NEW Protein Kinase Inhibitors for your Cell Signaling Research *(continued...)*

Cdk4 Inhibitor III

[5-(N-(4-Methylphenyl)amino)-2-methyl-4,7-dioxobenzothiazole]

A cell-permeable, selective Cdk4 inhibitor (IC_{50} = 6.0 µM for Cdk4/D1 and > 200 µM for Cdk2/A). Exhibits higher cytotoxicity against cancer cells (IC_{50} = 0.61, 1.08, 0.30, and 1.21 µg/ml against A 549, Col 1, HL-60, and HepG2 tumor cells, respectively) than Cisplatin (Cat. No. 232120). *Purity: ≥98% by HPLC.* M.W. 284.3



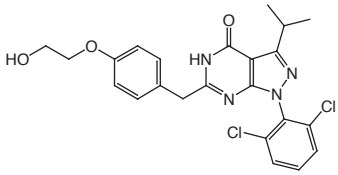
Cat. No. 219478 **5 mg** **€ 116**

Ref.: Ryu, C.K., et al. 2000. *Bioorg. Med. Chem. Lett.* **10,** 461.

Cdk/Crk Inhibitor

{1-(2,6-Dichlorophenyl)-1,5-dihydro-6-((4-(2-hydroxyethoxy)phenyl)methyl)-3-(1-methylethyl)-4H-pyrazolo[3,4-d]pyrimidin-4-one; RGB-286147}

A cell-permeable, potent, selective, and ATP-competitive inhibitor of Cdks (IC_{50} = 48 nM, 15 nM, 9 nM, 10 nM, 71 nM, and 9 nM for Cdk1/B, Cdk2/E, Cdk3/E, Cdk5/p35, Cdk7/H/MAT1, and Cdk9, respectively). Also inhibits Cdk4/D1, Cdk6/D3, and GSK-3β at higher concentrations (IC_{50} = 839 nM, 282 nM, and 754 nM, respectively). *Purity: ≥95% by HPLC.* M.W. 473.4



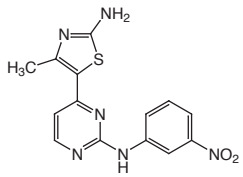
Cat. No. 219491 **1 mg** **€ 116**

Ref.: Caligiuri, M., et al. 2005. *Chem. Biol.* **12,** 1103.

Cdk2/9 Inhibitor

[(4-(2-Amino-4-methylthiazol-5-yl)pyrimidin-2-yl)-(3-nitrophenyl)amine]

A cell-permeable, potent, and ATP-competitive inhibitor of Cdk2/E and Cdk9/T1 (K_i = 2 nM and 4 nM, respectively). It also inhibits GSK-3β, $Cdk4/D_1$, Cdk7/H, Cdk1/B, and Abl at higher concentrations (K_i = 20, 53, 70, 80, and 160 nM, respectively). *Purity: ≥95% by HPLC.* M.W. 328.4



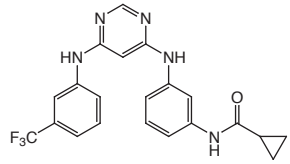
Cat. No. 238806 **5 mg** **€ 158**

Ref.: Kontopidis, G., et al. 2006. *Chem. Biol.* **13,** 201; Wang, S., et al. 2004. *J. Med. Chem.* **47,** 1662.

EGFR Inhibitor

[Cyclopropanecarboxylic acid-(3-(6-(3-trifluoromethyl-phenylamino)-pyrimidin-4-ylamino)-phenyl)-amide]

A cell-permeable, potent, ATP-competitive, and highly selective inhibitor of tyrosine kinase activity of EGFR and some EGFR mutants (IC_{50} = 21 nM, 63 nM, and 4 nM for EGFRwt, $EGFR^{L858R}$, and $EGFR^{L861Q}$, respectively). Shown to completely block EGF-induced EGFR autophosphorylation in U-2OS cells at 10 µM. *Purity: ≥97% by HPLC.* M.W. 413.4

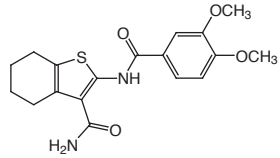


Cat. No. 324674 **1 mg** **€ 79**

Ref.: Zhang, Q., et al. 2006. *J. Am. Chem. Soc.* **128,** 2182

Flt-3 Inhibitor

A cell-permeable, potent, ATP-competitive, and highly selective Flt-3 inhibitor (IC_{50} = 42 nM) with little effect against a panel of 22 other kinases (IC_{50} ≥3 µM). Blocks the proliferation of human acute myelogenous leukemia cell line MV4-11 (IC_{50} = 340 nM) expressing constitutively active Flt-3. *Purity: ≥98% by HPLC.* M.W. 360.4



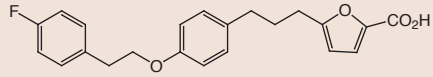
Cat. No. 343020 **5 mg** **€ 130**

Ref.: Patch, R.J., et al. 2006. *Bioorg. Med. Chem. Lett.* **16,** 3282.

AMPK Activator

[D942; 5-(3-(4-(2-(4-Fluorophenyl)ethoxy)phenyl)propyl)furan-2-carboxylic acid]

A cell-permeable, indirect activator of AMPK (AMP-activated Protein Kinase). Targets mitochondrial complex I, lowers extracellular ATP levels, and causes an elevation in cellular AMP levels. Shown to enhance glucose uptake in L6 myocytes (EC_{50} = 11.7 µM) in ZDF rats. *Purity: ≥95% by HPLC.* M.W. 368.4



Cat. No. 171256 **5 mg** **€ 126**

Ref.: Kosaka, T., et al. 2005. *Anal. Chem.* **77,** 2050.

NEW Protein Kinase Inhibitors for your Cell Signaling Research *(continued...)*

JNK Inhibitor VI, TI-JIP$_{153-163}$

(H_2N-RPKRPTTLNLF-NH_2; Truncated Inhibitor based on JNK-Interacting Protein 1)

A murine JIP-1 JNK-binding domain- (JBD) derived 11-mer peptide that directly interacts with JNK (K_d in low µM range) and specifically inhibits JNK activity without any inhibitory effects towards ERK or p38. The inhibition is not limited only to JBD-containing substrates and is found to be mixed/non-competitive with respect to ATP. JNK Inhibitor VII, TAT-TI-JIP$_{153-163}$, Cell-Permeable, is also available (Cat. No. 420134). *Purity:* ≥*97% by HPLC*. M.W. 1341.6

Cat. No. 420133 **2 mg** **€ 111**

Ref.: Barr, R.K., et al. 2004. *J. Biol. Chem.* **279,** 36327; Barr, R.K., et al. 2002. *J. Biol. Chem.* **277,** 10987.

JNK Inhibitor VII, TAT-TI-JIP$_{153-163}$, Cell-Permeable

(TAT_{38-48} -Truncated Inhibitor based on JNK-Interacting Protein 1; H_2N-YGRKKRRQRRR-RPKRPTTLNLF-NH_2)

The non-permeant JNK inhibitor peptide TI-JIP$_{153-163}$ (Cat. No. 420133) is made cell-permeable with an N-terminal TAT protein transduction domain sequence. Shown to offer neuroprotection in a rat ischemic brain injury model. *Purity:* ≥*97% by HPLC*. M.W. 2883.5

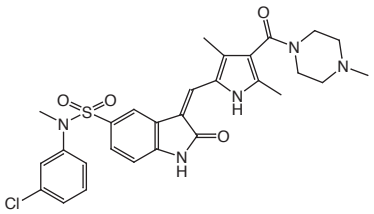
Cat. No. 420134 **2 mg** **€ 172**

Ref.: Guan, Q.H., et al. 2006. *Neuroscience*, **139,** 609; Barr, R.K., et al. 2004. *J. Biol. Chem.* **279,** 36327; Bogoyevitch, M.A., et al. 2003. *Cell. Mol. Biol. Lett.* **8,** 550; Barr, R.K., et al. 2002. *J. Biol. Chem.* **277,** 10987.

Met Kinase Inhibitor

[(3Z)-N-(3-Chlorophenyl)-3-((3,5-dimethyl-4-((4-methylpiperazin-1-yl)carbonyl)-1H-pyrrol-2-yl)methylene)-N-methyl-2-oxo-2,3-dihydro-1H-indole-5-sulfonamide; SU11274]

A cell-permeable, potent, reversible, and ATP-competitive inhibitor of Met kinase activity (IC_{50} = 20 nM). Exhibits > 60-fold selectivity over Flk and > 400-fold selectivity over Ron, FGFR-1, c-Src, Cdk2, PDGFRβ, EGFR, and Tie-2. Blocks met-mediated tumorigenesis in various cancer cell lines. *Purity:* ≥*98% by HPLC*. M.W. 568.1



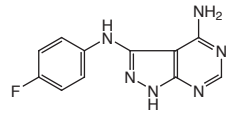
Cat. No. 448101 **1 mg** **€ 79**

Ref.: Ma. P. C., et al. 2005. *Cancer Res.* **65,** 1479; Berthou, S., et al. 2004. *Oncogene* **23,** 5387; Wang, X., et al. 2003. *Mol. Cancer Ther.* **2,** 1085; Sattler, M., et al. 2003. *Cancer Res.* **63,** 5462.

MNK1 Inhibitor

{4-Amino-5-(4-fluoroanilino)-pyrazolo[3,4-d]pyrimidine}

A cell-permeable, selective inhibitor of mitogen-activated protein kinase-interacting kinase 1 (MNK1; IC_{50} = 2.2 µM) with no inhibitory activity against p38, JNK1, ERK1/2, PKC, or Src-like kinases. *Purity:* ≥*98% by HPLC*. M.W. 244.2



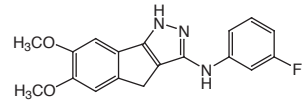
Cat. No. 454861 **5 mg** **€ 163**

Ref.: Topisirovic, I., et al. 2004. *Cancer Res.* **64,** 8639; Worch, J., et al. 2004. *Oncogene* **23,** 9162; Walsh, D., and Mohr, I. 2004. *Genes Dev.* **18,** 660; Morley, S.J., and Naegele, S. 2002. *J. Biol. Chem.* **277,** 32855; Knauf, U., et al. 2001. *Mol. Cell. Biol.* **21,** 5500.

PDGF Receptor Tyrosine Kinase Inhibitor IV

{3-Fluoro-N-(6,7-dimethoxy-2,4-dihydroindeno[1,2-c]pyrazol-3-yl)phenylamine}

A cell-permeable, ATP-competitive and reversible inhibitor of PDGFR tyrosine kinase (IC_{50} = 4.2 nM and 45 nM for -β and -α, respectively) and c-Abl (IC_{50} = 22 nM). *Purity:* ≥*98% by HPLC*. M.W. 325.3

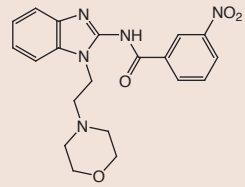


Cat. No. 521233 **1 mg** **€ 126**

Ref.: Ho, C.Y., et al. 2005. *J. Med. Chem.* **48,** 8163.

IRAK-1/4 Inhibitor

A cell-permeable, potent, and selective inhibitor of interleukin-1 receptor-associated kinases (IC_{50} = 300 nM and 200 nM for IRAK-1 and -4, respectively). Shown to exhibit little activity against a panel of 27 other kinases (IC_{50} >10 µM). *Purity:* ≥*95% by HPLC*. M.W. 395.4



Cat. No. 407601 **5 mg** **€ 79**

Ref.: Powers, J.P., et al. 2006. *Bioorg. Med. Chem. Lett.* **16,** 2842.

NEW Protein Kinase Inhibitors for your Cell Signaling Research *(continued...)*

Staurosporine, N-Benzoyl

(CGP 41 251; N-Benzoylstaurosporine)

A cell-permeable Staurosporine (Cat. No. 569397) that acts as a broad-spectrum, reversible, and ATP-competitive inhibitor of PKC (α, β, and γ), PDGFRβ, VEGFR2, Syk, PKCη, PKCδ, Flk-1, Flt3, Cdk1/B, PKA, c-Kit, c-Fgr, c-Src, VEGFR1, and EGFR (IC_{50} = 22 nM, 50 nM, 86 nM, 95 nM, 160 nM, 330 nM, 390 nM, 528 nM, 570 nM, 570 nM, 600 nM, 790 nM, 800 nM, 912 nM, and 1.0 µM, respectively). *Purity: ≥98% by HPLC.* M.W. 570.6

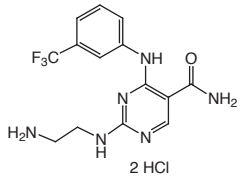
Cat. No. 539648 **1 mg** **€ 144**

Ref.: Weisberg, E., et al. 2002. *Cancer Cell* **1,** 433; Fabbro, D., et al. 2000. *Anticancer Drug Des.* **15,** 17; Meyer, T., et al. 1999. *Int. J. Cancer* **81,** 669; Meyer, T., et al. 1989. *Int. J. Cancer* **43,** 851.

Syk Inhibitor II

[2-(2-Aminoethylamino)-4-(3-trifluoromethylanilino)-pyrimidine-5-carboxamide, Dihydrochloride]

A cell-permeable, potent, selective and ATP-competitive inhibitor of Syk (IC_{50} = 41 nM). *Purity: ≥95% by HPLC.* M.W. 413.2



Cat. No. 574712 **1 mg** **€ 70**

Ref.: Hisamichi, H., et al. 2005. *Bioorg. Med. Chem.* **13,** 4936.

Lipid Hydroperoxide (LPO) Assay Kit

Format: Cuvette or 96-well plate

Assay range: 0.25 – 5 nmol hydroperoxide

Sample type: Tissues, cultured cells, plant materials, foods, biological fluids, etc.

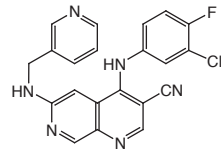
A sensitive and reliable assay kit for the measurement of the hydroperoxides from any sample containing lipid hydroperoxides, directly utilizing the redox reactions with ferrous ions. Quantification of lipid peroxidation is essential to assess the role of oxidative injury in pathophysiological disorders. Each kit is suitable for up to 100 assays. Can be used with tissues, cells, plant material, and biological fluids.

Cat. No. 437639 **1 kit** **€ 348**

Tpl2 Kinase Inhibitor

{4-(3-Chloro-4-fluorophenylamino)-6-(pyridin-3-yl-methylamino)-3-cyano-[1,7]-naphthyridine}

A cell-permeable, potent, reversible, and ATP-competitive inhibitor of Tpl2 kinase (IC_{50} = 50 nM). Displays significant selectivity over other related kinases (IC_{50} = 5, >40, 110, 180, >400, and >400 µM for EGFR, MEK, MK2, p38, Src, and PKC, respectively). *Purity: ≥95% by HPLC.* M.W. 404.8



Cat. No. 616373 **1 mg** **€ 116**

Ref.: Gavrin, L.K., et al. 2005. *Bioorg. Med. Chem. Lett.* **15,** 5288.

NEW Ready to use...

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: ≥95% by HPLC.* M.W. 551.6

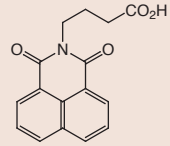
Cat. No. 124017 **1 mg** **€ 121**

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.

Virstatin

[4-(N-(1,8-Naphthalimide))-n-butyric acid]

A cell-permeable naphthalimide compound that inhibits virulence regulation in *Vibrio cholerae.* Shown to target the transcriptional regulator ToxT and prevent the expression of cholera toxin and the toxin coregulated pilus (TCP) with minimal bacterial toxicity. Effectively protects infant mice against TCP-dependent *V. cholerae* intestinal colonization *in vivo.* Displays minimal toxicity towards mammalian cells (up to 2 mM for Hep2 cells). *Purity: ≥97% by HPLC.* M.W. 283.3



Cat. No. 677520 **25 mg** **€ 83**

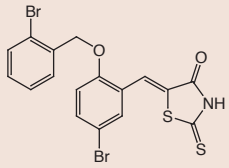
Ref.: Hung, D.T., et al. 2005. *Science* **310,** 670.

NEW Protein Phosphatase Inhibitors

PRL-3 Inhibitor

[1-(2-Bromobenzyloxy)-4-bromo-2-benzylidene rhodanine]

A cell-permeable, potent inhibitor of hPRL-3 (IC_{50} = 900 nM), a member of the regenerating liver family tyrosine phosphatases. Reduces the invasiveness of murine melanoma B16F10 cells. *Purity: ≥98% by HPLC.* M.W. 485.2



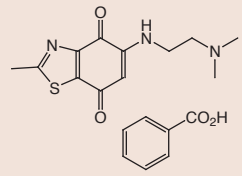
Cat. No. 539808 **10 mg** **€ 116**

Ref.: Ahn, J.H., et al. 2006. *Bioorg. Med. Chem. Lett.* **16,** 2996.

CDC25 Phosphatase Inhibitor III, BN82685, Benzoate Salt

[5-(2-Dimethylamino-ethylamino)-2-methyl-benzothiazole-4,7-dione, benzoate]

A cell-permeable, potent, selective, and irreversible inhibitor of CDC25 family phosphatases (IC_{50} = 109, 160, 249, 201, and 117 nM for 25A, 25B2, 25B3, 25C, and 25C-cat, respectively). *Purity: ≥98% by HPLC.* M.W. 387.5



Cat. No. 217693 **5 mg** **€ 135**

Ref.: Lavergne, O., et al. 2005. *Bioorg. Med. Chem. Lett.* **16,** 171; Brezak, M.C., et al. 2005. *Mol. Cancer Ther.* **4,** 1378.

NEW Proteases and Protease Inhibitors

Endopeptidase Lys-C, *Achromobacter lyticus*

Lysyl endopeptidase of the serine protease family that specifically hydrolyzes amide and peptide ester bonds at the carboxylic side of lysine and S-aminoethylcysteine residues. *Specific activity: ≥2 AU/mg protein.*

Cat. No. 324796 **2 U** **€ 139**

Ref.: Jekel, P.A., et al. 1983. *Anal. Biochem.* **134,** 347.

Plasmin, Human, Recombinant

(Fibrinolysin, Human, Recombinant; PL, Human, Recombinant)

Recombinant, human plasmin expressed in yeast as plasminogen and activated by urokinase treatment. Plasmin is a two-chain serine protease that catalyzes the hydrolysis of peptide bonds at the carboxylic acid side of arginine and lysine. Also cleaves fibrin clots, thus playing an important role in producing fibrin degradation products. *Specific activity: ≥ 20 units/mg protein. Purity: ≥95% by SDS-PAGE.*

Cat. No. 527622 **1 mg** **€ 417**

Ref.: Federici, A.B., et al. 1993. *Blood* **81,** 720; Hoffmann, J.J., and Janssen, W.C. 1992. *Thromb. Res.* **67,** 711.

MMP-13, Human, Recombinant, Active

Degrades a range of extracellular matrix proteins, including collagens, gelatin, aggrecan, perlecan and fibronectin. It is distinguished from other human collagenases by the fact that it also effectively degrades type II collagen. A biomarker for poor prognosis in many carcinomas and other type of cancers. *Specific activity: ≥50 mU/mg protein.*

Cat. No. 444287 **5 µg** **€ 228**

Ref.: Freije, M.P.S., et al. 1994. *J. Biol. Chem.* **269,**16766.

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 **10000 U** **€ 320**

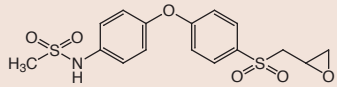
Ref.: Zhang, Y.M., et al. 1997. *J. Virol.* **71,** 6662; Chou, K.C., et al. 1996. *Proteins* **24,** 51; Krausslich, H.G., et al. 1995. *J. Virol.* **69,** 3407.

NEW Proteases and Protease Inhibitors *(continued...)*

MMP-2 Inhibitor II

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

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



Cat. No. 444286 **5 mg** **€ 130**

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

MMP-13 Inhibitor

Binds to the catalytic domain of MMP-13 and acts as a non-zinc chelating agent (IC_{50} = 8 nM). *Purity: ≥98% by HPLC.* M.W. 410.4

Cat. No. 444283 **1 mg** **€ 88**

InSolution™ TAPI-1

Supplied as a 10 mM (500 µg/100 µl) solution of TAPI-1 (Cat. No. 579051) in DMSO. *Purity: ≥97% by HPLC.* M.W. 499.6

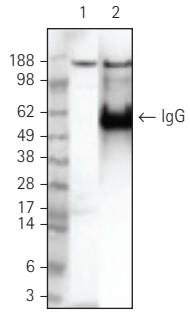
Cat. No. 579053 **500 µg** **€ 126**

NEW Tools for Apoptosis, Cell-Cycle, and Cancer Research

Anti-SLK Rabbit pAb

Liquid, immunoaffinity purified. Immunogen used was a synthetic peptide corresponding to amino acids derived from human SLK. Recognizes the ~145 kDa human SLK (Ste20-like kinase) protein in HeLa cells. Reacts with human. Suitable for immunoblotting and immunoprecipitation.

Cat. No. AP1039 **50 µg** **€ 126**



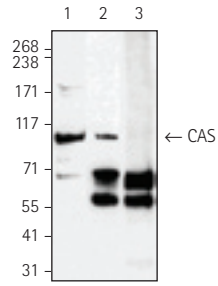
Lane 1: Detection of human SLK by immunoblotting. Sample: HeLa cell lysates (50 µg). Primary antibody: Anti-SLK pAb (Cat. No. AP1039) (3 µg/ml). Detection: chemiluminescence.

Lane 2: Detection of human SLK by immuno-precipitation followed by immunoblotting. Sample: HeLa cell lysates Primary antibody: Anti-SLK pAb (Cat. No. AP1039) (5 µg/500 µg total protein in 500 µl).

Anti-CAS Rabbit pAb

Liquid, immuno-affinity purified. Immunogen used was a synthetic peptide corresponding to amino acids at the N-terminus of human CAS. Recognizes a 100 kDa cellular apoptosis susceptibility (CAS) protein. Reacts with human. Suitable for immunoblotting and immunoprecipitation.

Cat. No. AP1045 **50 µg** **€ 126**



Lane 1: Detection of human CAS by immunoblotting. Sample: HeLa cell lysate (50 µg). Primary antibody: Anti-CAS Rabbit pAb (Cat. No. AP1045) (1 µg/ml). Detection: chemiluminescence.

Lanes 2 and 3: Detection of human CAS by immuno-precipition followed by immunoblotting. Sample: HeLa cell lysate (50 µg). Primary antibody: Anti-CAS Rabbit pAb (Cat. No. AP1045) (3 µg/mg protein) and Rabbit IgG (3 µg/mg protein).

Annexin V-PE Apoptosis Detection Kit

Format: Flow cytometry, fluorescence microscopy

A convenient kit useful for the identification of phosphatidylserine (PS) that is translocated from the cytoplasmic face of the plasma membrane to the cell surface during apoptosis. Annexin V has a strong natural affinity for PS, hence, it is used for detecting apoptosis. This assay can be performed on live cells.

Cat. No. CBA060 **25 tests** **€ 153**
100 tests **€ 260**

InSolution™ Caspase Inhibitor VI

A 10 mM (1 mg/221 µl) solution of Caspase Inhibitor VI (Cat. No. 219007) in DMSO. *Purity: ≥95% by TLC.* M.W. 453.5

Cat. No. 219011 **1 mg** **€ 164**

NEW Tools for Apoptosis, Cell-Cycle, and Cancer Research *(continued...)*

p21-Activated Kinase Inhibitor, PAK18

(PAK Inhibitor, PAK18; H_2N-RKKRRQRRR~G~PPVIAPRPEHTKSVYTRS-CO_2H)

A PAK (p21-activated kinase) inhibitor peptide composed of the cell permeant TAT peptide sequence and an 18-mer Pro-rich PIX-interacting motif of PAK that disrupts PIX-PAK interaction. Reduces cellular PAK phosphorylation and induces neurodegenerative morphology in hippocampal neurons *in vitro*. PIX-interacting motif sequence has also been shown to block ras-dependent tumor growth and PAK activation in NIH-3T3 cells. The inactive control peptide, PAK18-R192A, is also available (Cat. No. 506102). *Purity: ≥97% by HPLC.* M.W. 3413.9

Cat. No. 506101 **2 mg** **€ 200**

Ref.: Zhao, L., et al. 2006. *Nat. Neurosci* **9,** 234; Maruta, H., et al. 2002. *Methods Mol. Biol.* **189,** 75.

p21-Activated Kinase Inhibitor, Negative Control

(PAK18-R192A; H_2N-RKKRRQRRR~G~PPVIAPAPEHTKSVYTRS-CO_2H)

The p21-Activated Kinase Inhibitor, PAK18 (Cat. No. 506101), with single amino acid mutation R192A, serves as an inactive control peptide for PAK 18. *Purity: ≥97% by HPLC.* M.W. 3328.8

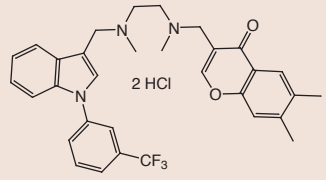
Cat. No. 506102 **2 mg** **€ 200**

Ref.: Zhao, L., et al. 2006. *Nat. Neurosci* **9,** 234; Maruta, H., et al. 2002. *Methods Mol. Biol.* **189,** 75.

TNF-α Inhibitor

[6,7-Dimethyl-3-((methyl-(2-(methyl-(1-(3-trifluoromethyl-phenyl)-1H-indol-3-ylmethyl)-amino)-ethyl)-amino)-methyl)-chromen-4-one, diHCl]

Inactivates TNF-α by non-covalently binding to the TNF-α trimer and promotes subunit dissociation and prevents TNF-α binding to its receptor (IC_{50} = 22 µM). *Purity: ≥98% by HPLC.* M.W. 629.6



Cat. No. 654256 **5 mg** **€ 172**

Ref.: He, M.M., et al. 2005. *Science* **310,** 1022.

p53 Activator III, RITA

[2,5-*bis*-(5-Hydroxymethyl-2-thienyl)-furan; NSC 652287; Reactivation of p53 and Induction of Tumor cell Apoptosis]

A cell-permeable, p53-targeting tricyclic thiophene derivative that blocks p53—MDM2 interaction and p53 ubiquitination. Induces p53-dependent apoptosis in tumor cells expressing wild-type p53. Restores tumor suppressor function of p53. *Purity: ≥97% by HPLC.* M.W. 292.4

Cat. No. 506149 **1 mg** **€ 70**

Ref.: Grinkevich, V., et al. 2005. *Nat. Med.* **11,** 1136; Krajewski, M., et al. 2005. *Nat. Med.* **11,** 1135; Issaeva, N., et al. 2004. *Nat. Med.* **10,** 1321; Nieves-Neira, W., et al. 1999. *Mol. Pharmacol.* **56,** 478; Rivera, M.I., et al. 1999. *Biochem. Pharmacol.* **57,** 1283.

Fumitremorgin C, *Aspergillus. fumigatus*

(FTC; NSC719655)

A cell-permeable, inhibitor of BCRP/ABCG2 (breast cancer resistance protein/ATP-binding cassette G2) multidrug transport activity. Also acts as a potent and specific chemosenzitizing agent. *Purity: ≥95% by HPLC.* M.W. 379.5

Cat. No. 344847 **250 µg** **€ 139**

Ref.: Allen, J.D., et al. 2002. *Mol. Cancer Ther.* **1,** 417; Ozvegy, C., et al. 2001. *Biochem. Biophys. Res. Commun.* **285,** 111; Rabindran, S.K., et al. 2000. *Cancer Res.* **60,** 47; Rabindran, S.K., et al. 1998. *Cancer Res.* **58,** 5850; Cole, R.J., et al. 1977. *J. Agric. Food Chem.* **25,** 826.

Bcl-2 Inhibitor III, EM20-25

[5-(6-Chloro-2,4-dioxo-1,3,4,10-tetrahydro-2H-9-oxa-1,3-diaza-anthracen-10-yl)-pyrimidine-2,4,6-trione]

A cell-permeable pyrimidine-trione compound that sensitizes apoptosis-resistant, Bcl-2-overexpressing leukemic cells to cytotoxic drugs. Binds to Bcl-2 and disrupts its interaction with Bax and activates caspase-9. Also induces PTP (permeability transition pore) opening in both isolated mitochondria and intact cells, without affecting respiration. *Purity: ≥95% by elemental analysis.* M.W. 376.7

Cat. No. 197332 **10 mg** **€ 79**

Ref.: Milanesi, E., et al. 2006. *J. Biol. Chem.* **281,** 10066.

NEW Tools for Apoptosis, Cell-Cycle, and Cancer Research *(continued...)*

TRAIL, Human, Recombinant, *E. coli*

(Apo2L, Human, Recombinant, *E. coli*; TNF-Related Apoptosis-Inducing Ligand, Human, Recombinant, *E. coli*)

Soluble, recombinant, human TRAIL (amino acids 114-281) and expressed in *E. coli*. Ligand for TRAIL receptors DR4 and DR5. Displays potent antitumor activity against selected targets and induces apoptosis in a number of transformed cell lines. *Purity: ≥95% by SDS-PAGE.*
M.W. 18,000

Cat. No. 616374 **100 µg** **€ 315**

Ref.: Lin, Y., et al. 2000. *Mol. Cell. Biol.* **20,** 6638; Mitsaides, N., et al. 2000. *Cancer Res.* **60,** 4122; Griffith, T.S., et al. 1999. *J. Exp. Med.* **189,** 1343; Pan, G., et al. 1997. *Science* **276,** 111; Pan, G., et al. 1997. *Science* **277,** 815; Sheridan, J.P., et al. 1997. *Science* **277,** 818; Pitti, R.M., et al. 1996. *J. Biol. Chem.* **271,** 12687;

cIAP-1, Human, Recombinant, *E. coli*

(HIAP-2; MIHB)

A recombinant human cIAP-1 expressed in *E. coli*. Inhibits proteolytic activity of mature caspases by interacting with their BIR domain. *Purity: ≥ 85% by SDS-PAGE.*
M.W. 72,300

Cat. No. 539661 **50 µg** **€ 283**

Ref.: Herrera, B., et al. *FEBS Lett.* **520,** 93; Deveraux, Q.L. and Reed, J.C. 1999. *Genes Dev.* **13,** 239; Deveraux, Q.L., et al. 1997. *Nature* **388,** 300; Roy, N., et al. 1997. *EMBO J.* **16,** 6914.

Histone Deacetylase, Human, Recombinant, *S. frugiperda*

(HDAC3, Human, Recombinant)

Recombinant human HDAC3 expressed in insect cells using a baculovirus expression system. A class I histone deacetylase that regulates gene expression by deacetylating of histones and nonhistone proteins. *Purity: ≥95% by SDS-PAGE.* M.W. 47,000

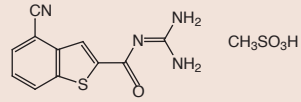
Cat. No. 382169 **5000 U** **€ 320**

Ref.: Zhang, X., et al. 2005. *Genes Dev.* **19,** 827; Dangond, F., et al. 1998. *Biochem. Biophys. Res. Commun.* **242,** 648; Yang, W.M., et al. 1997. *J. Biol. Chem.* **272,** 28001.

Na^+/H^+ Exchanger Isoform-1 Inhibitor

{(4-Cyanobenzo[b]thiophene-2-carbonyl)guanidine, methanesulfonate; NHE-1 Inhibitor}

A cell-permeable acylguanidine compound that inhibits NHE-1 with an IC_{50} of 2.0 µM in PS120 variant cells expressing hNHE-1. Shown to offer cardioprotection in rat models of myocardial ischemia and reperfusion. *Purity: ≥97% by HPLC.* M.W. 340.4



Cat. No. 567500 **5 mg** **€ 83**

Ref.: Lee, S., et al. 2005. *Bioorg. Med. Chem. Lett.* **15,** 2998.

NEW Steroid Receptor Modulators

GPR30 Agonist, G-1

{1-(4-(6-Bromobenzo[1,3]dioxol-5-yl)-3a,4,5,9b-tetrahydro-3H-cyclopenta[c]quinolin-8-yl)-ethanone}

A cell-permeable, nonsteroidal, dihydroquinoline compound that acts as a high-affinity agonist for GPR30, the G protein-coupled transmembrane estrogen receptor in ER. Specifically competes with estrogen-binding to GPR30 (K_i = 11 nM), but not to the classical nuclear-residing estrogen receptors, ERα and ERβ. *Purity: ≥98% by HPLC.*
M.W. 412.3

Cat. No. 371705 **5 mg** **€ 107**

Ref.: Bologa, C.G., et al. 2006. *Nat. Chem. Biol.* **2,** 207.

Glucocorticoid Receptor Modulator, CpdA

[2-((4-Acetoxyphenyl)-2-chloro-N-methyl)ethylammonium chloride]

A cell-permeable aziridine precursor that acts as a ligand for nonsteroidal glucocorticoid receptor (Cat. No. 346100) ligand with a 4-fold higher binding affinity than that of Dexamethasone (Cat. No. 265005). Induces GR nuclear translocation and selectively activates GR-mediated transrepression of the NF-κB-dependent production of pro-inflammatory cytokines. *Purity: ≥97% by HPLC.*
M.W. 264.2

Cat. No. 346110 **25 mg** **€ 111**

Ref.: De Bosscher, K., et al. 2005. *Proc. Natl. Acad. Sci. USA* **102,** 15827.

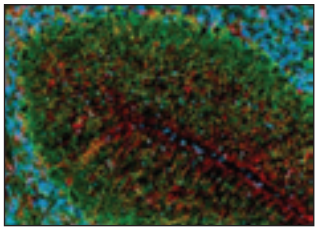
Neurochemical Corner

Anti-GFAP Cocktail Mouse mAb (SMI-22)

Undiluted ascites. Immunogen used as purified bovine GFAP protein. Recognizes ~50 kDa glial fibrillary acidic protein (GFAP) in human and bovine cytoskeletal preparations. Reacts with a wide variety of species. Suitable for **ELISA, FS, IB, IC, PS**

Cat. No. NE1015 **100 µl** **€ 246**

Ref.: Vick, W.W., et al. 1987. *Acta. Cytol.* **31,** 816; McLendon R.E., et al. 1986. *J. Neuropathol. Exp. Neurol.* **45,** 692; Pegram, C.N., et al. 1985. *Neurochem. Pathol.* **3,** 119.



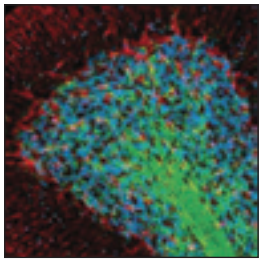
Detection of glial fibrillary acidic protein by staining frozen section of rat brain. Primary antibody: Anti GFAP Cocktail Mouse mAb (SMI-22) (Cat. No. NE1015) (1:1000). Detection: fluorescence (red) with Hoechst 33342 counterstain.

Anti-Myelin CNPase Mouse mAb (SMI-91)

Undiluted ascites. Immunogen used was purified human myelin CNPase protein. Recognizes the ~46 and ~48 kDa subunits of the 94 kDa myelin CNPase dimer in rat brain extracts. Reacts with bovine, canine, human, mouse, porcine, rat, and sheep. Suitable for **ELISA, FS, IB, IC, PS**

Cat. No. NE1020 **100 µl** **€ 246**

Ref.: Sprinkle, T.J., 1989. *Crit. Rev. Neurobiol.* **4,** 235.



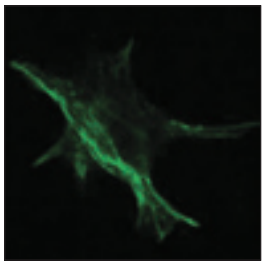
Detection of myelin CNPase by staining frozen section of rat brain. Primary antibody: Anti-Myelin CNPAse mAb (SMI-91) (Cat. No. NE1020) (1:1000). Detection: fluorescence (red) with Hoechst 33342 counterstain.

Anti-Nestin Mouse mAb (2C13B9)

Liquid, purified. Immunogen uses was a GST-fusion protein containing amino acids 1464-1614 of human nestin. Recognizes the ~220-240 kDa Nestin protein in U251 cells. Suitable for **FS, IB, IC**

Cat. No. ST1111 **100 µl** **€ 218**

Ref.: Humphrey, R.K., et al. 2003. *Diabetes* **52,** 2519; Messam, C.A., et al. 2000. *Exp. Neurol.* **161,** 585.



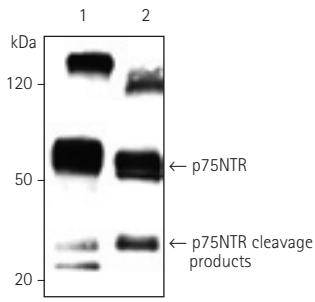
Detection of human nestin by immunocytochemistry. Sample: U251 cells fixed in methanol. Primary antibody: Anti-Nestin mAb (2C13B9) (Cat. No. ST1111) (1:200). Detection: fluorescence (green).

Anti-p75 Neurotrophin Receptor Rabbit pAb

Liquid, purified. Immunogen used was a recombinant protein containing amino acids 273-425 of rat p75NTR. Recognizes the ~75 kDa neurotrophin receptor (p75NTR) protein in cultured mouse fibroblasts stably transfected with human p75NTR. Also recognizes additional lower MW proteins that are cleavage products of p75NTR. Suitable for **IB, IC**

Cat. No. NE1024 **100 µl** **€ 320**

Ref.: Kanning, K.C., et al. 2003. *J. Neurosci.* **23,** 5425.



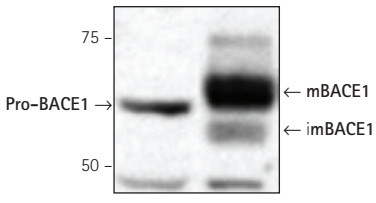
Detection of human p75 neurotrophin receptor by immunoblotting. Sample: Cell lysates (30 µg) from mouse fibroblasts stably transfected with human p75NTR (lane 1) and KEK293 cells, transiently transfected with human p75 NTR (lane 2). Primary antibody: Anti-p75 Neurotrophin Receptor Rabbit pAb (Cat. No. NE1024) (1-2 µg/ml). Detection: chemiluminescence.

Anti-ProBACE1 (24-45) Rabbit pAb

Undiluted serum. Immunogen used was a synthetic peptide corresponding to amino acids 24-45 of human proBACE1. Recognizes the ~60 kDa proBACE1 protein in N2a cells. Reacts with human, mouse, and rat. Suitable for **IB, IC, IP**

Cat. No. NE1025 **100 µl** **€ 320**

Ref.: Yan, R., et al. 2001. *J. Biol. Chem.* **276,** 36788.



Detection of mouse proBACE by immunoblotting. Sample: N2a cell lysates. Primary antibodies: Anti-ProBace 1 (24-45) Rabbit pAb (Cat. No. NE1025) (1:1000) (left lane) and anti-BACE1 (right lane). Detection: chemiluminescence. Photo: courtesy of X. Hu, The Burnham Institute, San Diego.

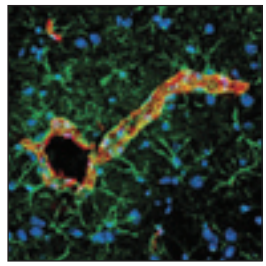
Neurochemical Corner *(continued...)*

Anti-Rat Blood-Brain Barrier Mouse mAb (SMI-71)

Undiluted ascites. Immunogen used was homogenized hypothalamic extracted from Fischer 344 rats. Recognizes an endothelial protein found in blood-brain or blood-nerve barriers in rat. Suitable for **ELISA, FS, PS**

Cat. No. NE1026 **100 µl** **€ 246**

Ref.: Hanu, R., et al. 2000. *Am. J. Physiol. Cell Physiol.* **278,** 921; Sternberger, N.H., et al. 1989. *J. Neuroimmunol.* **21,** 241; Sternberger, N.H., et al. 1987. *Proc. Natl. Acad. Sci. USA* **84,** 8169.



Detection of blood-barrier protein by staining frozen section of rat brain. Primary antibody: Anti-Rat Blood-Brain Barrier Mouse mAb (SMI-71) (Cat. No. NE1026) (1:1000). Detection: fluorescence (red) with Hoechst 33342 counterstain.

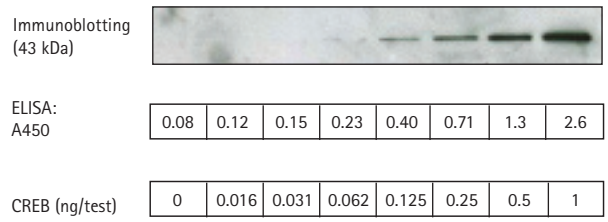
NEW Transcription Factor Assay Kits

CREB ELISA Kit

Format: 96-well plate
Sensitivity: < 0.025 ng/ml
Assay time: 0.156-10 ng/ml

A solid phase sandwich ELISA kit suitable for detection and quantitation of CREB (cAMP-Response Element-Binding protein) levels independent of its phosphorylation state in human and mouse cells. Suitable for use with human and mouse samples.

Cat. No. CBA071 **1 kit** **€ 534**



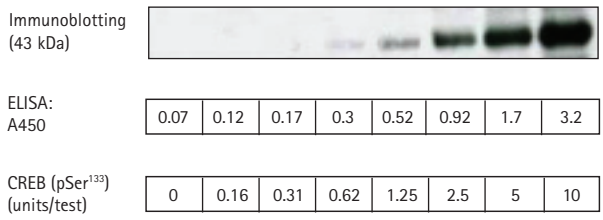
The sensitivity of this ELISA was compared to immunoblotting using known quantities of CREB. ELISA sensitivity was determined to be about four times greater than that of immunoblotting.

PhosphoDetect™ CREB (pSer^{133}) ELISA Kit

Format: 96-well plate
Sensitivity: < 0.9 unit/ml
Assay range: 1.6-100 units/ml

A solid phase sandwich ELISA kit suitable for detection and quantitation of CREB (cAMP-Response Element-Binding protein) phosphorylated at Ser^{133} in human and mouse cells. Suitable for use with human and mouse samples.

Cat. No. CBA072 **1 kit** **€ 534**



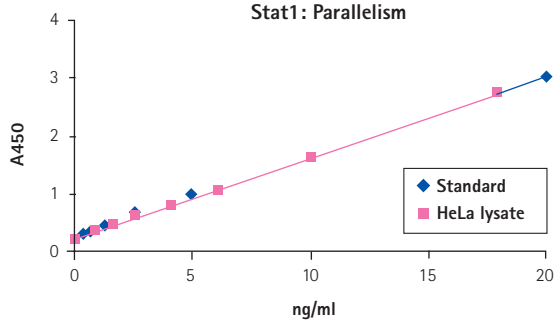
The sensitivity of this ELISA was compared to immunoblotting using known quantities of CREB (pSer^{133}). The bands shown in the immunoblot were developed using rabbit anti-CREB (pSer^{133}) and an alkaline phosphatase conjugated anti-rabbit IgG followed by chemiluminescent detection.

STAT1 ELISA Kit

Format: 96-well plate
Sensitivity: < 0.27 ng/ml
Assay range: 0.3-20 ng/ml

A solid phase sandwich ELISA kit suitable for detection and quantitation of STAT1 levels independent of its phosphorylation state. This kit is designed for use with human cells and tissues.

Cat. No. CBA034 **1 kit** **€ 725**



HeLa cell lysates were serially diluted in standard diluent buffer and STAT1 levels were measured. The absorbance of each diluted sample was plotted against the STAT1 standard curve.

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NEW Antibodies for Transcription Factors

PhosphoDetect™ STAT Antibody Sampler Kit

Polyclonal anti-STAT antibodies supplied as 40 µl each. A convenient set of affinity purified antibodies useful for evaluating the activation status of various STAT proteins, including the phosphorylation of STAT1 at Tyr^{701}, STAT2 at Tyr^{690}, STAT3 at Tyr^{705}/Ser^{727}, STAT5 at Tyr^{694} and STAT6 at Tyr^{641}. Immunogen used were a series of synthetic peptides corresponding to amino acids surrounding the designated phosphorylation sites of STAT1, STAT2, STAT3, STAT5, and STAT6, each coupled to KLH. Useful for a variety of applications.

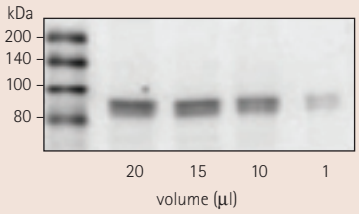
Cat. No. PS1021 **1 kit** **€ 417**

Anti-STAT5 Rabbit pAb

Liquid, protein A and immunoaffinity purified. Immunogen used was a synthetic peptide corresponding to amino acids surrounding residue 260 of human STAT5, coupled to KLH. Recognizes the ~90 kDa STAT5α and STAT5β (doublet) proteins in K562 cells. Reacts with human and mouse. Suitable for immunoblotting and immunoprecipitation

Cat. No. ST1105 **50 µl** **€ 126**

Ref.: Demoulin, J.B., et al. 1999. *J. Biol. Chem.* **274,** 25855; Dentelli, P., et al. 1999. *J. Immunol.* **163,** 2151; Meinke, A., et al. 1996. *Mol. Cell. Biol.* **16,** 6937; Gouilleux, F., et al. 1994. *EMBO J.* **13,** 4361; Wakao, H., et al. 1994. *EMBO J.* **13,** 2182.



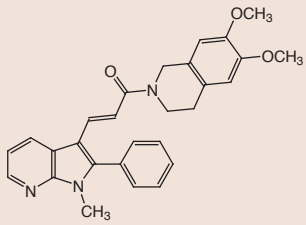
Detection of human STAT5 by immunoblotting. Sample: K562 cell lysates. Primary antibody: Anti-STAT5 Rabbit pAb (Cat. No. ST1105) (1:1000). Detection: chemiluminescence.

Transcription Factor Inhibitors

Smad3 Inhibitor, SIS3

{6,7-Dimethyl-2-((2E)-3-(1-methyl-2-phenyl-1H-pyrrolo[2,3-b]pyridin-3-yl-prop-2-enoyl))-1,2,3,4-tetrahydroisoquinoline; Specific Inhibitor of Smad3}

A cell-permeable pyrrolopyridine compound that selectively inhibits TGF-β1-dependent Smad3 phosphorylation and Smad3-mediated cellular signaling with no effect on Smad2, p38 MAPK, ERK, or PI 3-K signaling. *Purity: ≥95% by HPLC.* M.W. 453.5



Cat. No. 566405 **1 mg** **€ 107**

Ref.: Jinnin, M., et al. 2006. *Mol. Pharmacol.* **69,** 597.

PPARγ Antagonist III, G3335

(H-Trp-Glu-OH)

A cell-permeable dipeptide that acts as a selective and reversible PPARγ antagonist (K_D ~ 8 µM). Shown to inhibit the agonist activity of Rosiglitazone (100 nM) in a dose-dependent manner (IC_{50} = 31.9 µM) in transfected COS-7 cells. *Purity: ≥97% by elemental analysis.* M.W. 333.3

Cat. No. 516566 **50 mg** **€ 74**

Ref.: Ye, F., et al. 2006. *Chembiochem* **7,** 74.

NEW Cell Adhesion Research Tools

Anti-Paxillin Mouse mAb (M107)

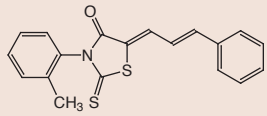
Liquid, protein A purified. Immunogen used was a full-length recombinant human paxillin. Recognizes the ~68 kDa paxillin protein in A431 cells. Reacts with chicken, human, mouse, and rat. Suitable for ELISA, immunoblotting, immunocytochemistry, and immunoprecipitation.

Cat. No. CB1016 **50 µl** **€ 181**

Integrin $\alpha_M\beta_2$ Ligand

[IMB-10; 3-(*o*-Tolyl)-5-(3-phenyl-2-propenylidene)-2-thioxo-1,3-thiazolin-4-one]

A cell-permeable thioxothiazolidine compound that increases cell adhesion and lowers leukemia cell migration *in vitro* and leukocyte recruitment *in vivo*. Binds to and stabilizes integrin α_M I domain active conformation and enhances the ligand (pro-MMP-9 and fibrinogen) binding ability. *Purity: ≥98% by HPLC.* M.W. 337.5



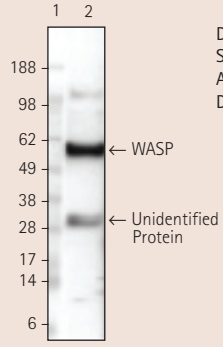
Cat. No. 407271 **5 mg** **€ 79**

Ref.: Bjorklund, M., et al. 2006. *Biochemistry* **45,** 2862.

Anti-WASP Rabbit pAb

Liquid, immunoaffinity purified. Immunogen used was a synthetic peptide corresponding to the N-terminal region of human WASP. Recognizes the ~60 kDa WASP protein in U937 cells. Reacts with human. Suitable for immunoblotting.

Cat. No. ST1113 **50 µg** **€ 126**



Detection of human WASP by immunoblotting. Sample: U937 cell lysates (50 mg). Primary antibody: Anti-WASP Rabbit pAb (Cat. No. ST1113) (0.3 µg/ml). Detection: Chemiluminescence.

Interested in Proteasome/Ubiquitination Research?

FAT10, His•Tag®, Human, Recombinant, *E. coli*

(Diubiquitin)

Human, recombinant FAT10 expressed in *E. coli* with an N-terminal His•Tag® sequence. FAT10 is a small ubiquitin-like protein whose expression is synergistically inducible with γ-interferon and TNF-α. Composed of two ubiquitin-like domains and bears a di-glycine motif at the C-terminus. The wild-type form of FAT10 (but not the di-glycine form) has been shown to conjugate to target proteins. Expression of FAT10 is reported to cause apoptosis. *Purity: ≥95% by SDS-PAGE.*

Cat. No. 662077 **100 µg** **€ 139**

Ref.: Hipp, M.S., et al. 2004. *J. Biol. Chem.* **279,** 16503; Lee, C.G., et al. 2003. *Oncogene* **22,** 2592; Raasi, S., et al. 2001. *J. Biol. Chem.* **276,** 35334; Liu, Y.C., et al. 1999. *Proc. Natl. Acad. Sci. USA* **96,** 4313.

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

(Ubiquitin-conjugating enzyme E2 E2, Human, Recombinant, *S. frugiperda*)

Recombinant, human, UbcH8 conjugating enzyme fused to GST and expressed in Sf9 insect cells using a baculovirus expression system. A member of the E2 family of ubiquitin conjugating enzymes. *Purity: ≥95% by SDS-PAGE.*

Cat. No. 662082 **100 µg** **€ 228**

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.

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Proteasome/Ubiquitination *(continued...)*

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

(Smad ubiquitination regulatory factor 2 Ligating Enzyme, Human, Recombinant, *S. frugiperda*)

Recombinant, human Smad ubiquitination regulatory factor 2 (Smurf2) expressed in Sf9 insect cells using a baculovirus expression system. Smurf2 is an E3 ubiquitin ligase that is 83% identical to Smurf1. Smurf2 is known to be constitutively associated with Smad7. While Smurf2 is typically found in the nucleus, binding to Smad7 induces export and recruitment to the activated transforming growth factor-β receptor (TGFBR), where it causes degradation of receptors and Smad7 via proteasomal and lysosomal pathways. *Purity: ≥98% by SDS-PAGE.*

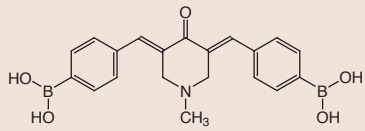
Cat. No. 662079 **10 µg** **€ 394**

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.

Proteasome Inhibitor IX, AM114

[3,5-*bis*-(4-Boronic acid-benzylidene)-1-methylpiperidin-4-one]

A cell-permeable boronate chalcone compound with ~ 30-fold higher potency than MG-132 (Cat. No. 474790) in inhibiting 20S proteasome chymotrypsin-like activity (IC_{50} ~ 1 µM). *Purity: ≥95% by HPLC.* M.W. 377



Cat. No. 539184 **10 mg** **€ 111**

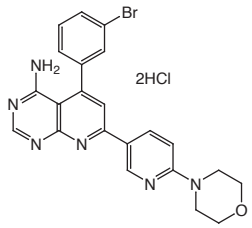
Ref.: Achanta, G., et al. 2006. *Mol. Pharmacol.* **70,** 426.

NEW Tools for the Study of Diabetes and Insulin Signaling

Adenosine Kinase Inhibitor

{ABT-702; 4-Amino-5-(3-bromophenyl)-7-(6-morpholino-pyridin-3-yl)pyrido[2,3-d]pyrimidine, 2HCl}

A cell-permeable, potent, adenosine-competitive, and reversible adenosine kinase (AK) inhibitor (IC_{50} = 50.7 nM using intact IMR-32 cells and 1.7 nM in cell-free assays using rat brain cytosolic AK). The inhibitory effect is not species-specific and its pharmacological selectivity is confirmed using a panel of more than 80 other enzymes, ion channels, and receptors, including various adesine receptors. It readily crosses the blood-brain barrier and is shown to be efficacious in *in vivo* animal models via various administration methods (i.p., p.o., s.c.) *Purity: ≥98% by HPLC.* M.W. 536.3



Cat. No. 116890 **5 mg** **€ 172**

Ref.: De Vry, J., et al. 2004. *Eur. J. Pharmacol.* **491,** 137; Boyle, D.L., et al. 2001. *J. Pharmacol. Exp. Ther.* **296,** 495.

Glycogen Synthase Kinase 3β-Isozyme, Rabbit Skeletal Muscle, Recombinant, *E. coli*

(GSK 3β-Isozyme, Rabbit Skeletal Muscle, Recombinant, *E. coli*)

Dual specificity kinase. One of several protein kinases that phosphorylates glycogen synthase and a variety of other substrates, including $p90^{rsk}$, Tau, c-Jun, and CREB. Plays a key role in Wnt and insulin signaling. Specific activity: ≥5,000,000 units/mg protein.

Cat. No. 361526 **5 KU** **€ 302**

Ref.: Dajani, R., et al. 2001. *Cell* **105,** 721; Wang, Q.M., et al. 1995. *Biochem. Biophys. Res. Commun.* **208,** 796; Fiol, C.J., et al. 1994. *J. Biol. Chem.* **269,** 32187; Wang, Q.M., et al. 1994. *J. Biol. Chem.* **269,** 14566; Ishiguro, K., et al. 1993. *FEBS Lett.* **325,** 167.

Glycogen Synthase Kinase 3β-Isozyme, His•Tag®, Human, Recombinant, *E. coli*

(GSK-3β; Tau Protein Kinase I; TPK I)

A dual specificity kinase that plays important roles in insulin- and Wnt-signalings. Also plays a major role in destablizing microtubule stability by its ability to phosphorylate tau. This recombinant kinase contains both an N- and a C-terminal His•Tag® sequence. *Purity: ≥90% by SDS-PAGE.*

Cat. No. 361524 **100 µg** **€ 404**

Ref.: Harwood, A., and Braga, V.M. 2003. *Nat. Cell Biol.* **5,** 275; Bhat, R.V., and Budd, S.L. 2002. *Neurosignals* **11,** 251.

NEW Tools for the Study of Diabetes and Insulin Signaling *(continued...)*

Glycogen Phosphorylase Inhibitor

[1-(3-(3-(2-Chloro-4,5-difluorobenzoyl)ureido)-4-methoxyphenyl)-3-methylurea]

A cell-permeable, potent, and AMP-competitive inhibitor of glycogen phosphorylase (IC_{50} = 53 nM). Inhibits glucagon-induced glycogenolysis in hepatocytes (IC_{50} = 380 nM) *in vitro* and *in vivo*. *Purity: ≥98% by HPLC*. M.W. 412.8.

Cat. No. 361515 **1 mg** **€ 65**

Ref.: Klabunde, T., et al. 2005. *J. Med. Chem.* **48,** 6178

IGF-1R Inhibitor II

[N-(2-Methoxy-5-chlorophenyl)-N´-(2-methylquinolin-4-yl)-urea]

A cell-permeable phenylquinolinyl-urea compound that inhibits IGF-1R autophosphorylation (IC_{50} = 12 µM in inhibiting ligand-induced autophosphorylation in MCF-7 cells and < 1 µM in a cell-free kinase assay). Reduces IGF-1R-dependent tumor cell growth both *in vitro* (IC_{50} = 8 and 15 µM for MCF-7 and MCNeuA, respectively). *Purity: ≥98% by HPLC*. M.W. 341.8.

Cat. No. 407248 **10 mg** **€ 116**

IRS1-p30, Human, Recombinant, *E. coli*

(Insulin Receptor Substrate-1 p30, Human, Recombinant, *E. coli*)

Recombinant, human insulin receptor substrate 1 consisting of the p30 fragment (IRS1p30, amino acids 516-777) expressed in *E. coli*. This recombinant p30 fragment contains 5 potential tyrosine phosphorylation sites; phosphorylated IRS1p30 will bind to insulin receptor. *Purity: >95% by SDS-PAGE*.

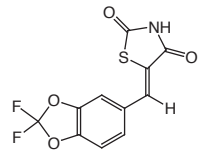
Cat. No. 663001 **150 µg** **€ 506**

Ref.: Yong, W., et al. 2004. *Acta Physiol. Sinica* **56,** 539; Siemeister, et al. 1995. *J. Biol. Chem.* **270,** 4870.

PI 3-Kγ Inhibitor II

{5-(2,2-Difluoro-benzo[1,3]dioxol-5-ylmethylene)-thiazolidine-2,4-dione}

A cell-permeable, potent, and ATP-competitive inhibitor of PI 3-Kγ (K_i = 180 nM; IC_{50} = 250 nM). Exhibits great selectivity over PI 3-Kα (IC_{50} = 4.5 µM), PI 3-Kβ, and PI 3-Kδ (IC_{50} >20 µM), and shows little effect towards 38 commonly studied kinases. Exhibit better *in vivo* efficacy than LY294002 (Cat. No. 440202 and 440204). *Purity: ≥98% by HPLC*. M.W. 285.2



Cat. No. 528108 **5 mg** **€ 126**

Optimize your Protein Digestion

NEW ProteoExtract® Tryptic Cleavage Modification Kit

Format: Microcentrifuge tube
Assay time: 8-24 h
Sample type: In-gel protein

This kit utilizes specific chemical modifications to control the trypsin cleavage site during in-gel digestions. In combination with the ProteoExtract® All-in-One Trypsin Digestion Kit (Cat. No. 650212) the resulting sample contains either Arg C-like or Lys C-like digested peptide fragments for further analysis, such as mass spectrometry. Each kit is suitable for up to 100 assays.

Cat. No. 539182 **1 kit** **€ 121**

Transdermal Hormone Delivery Peptide, TD-1

(H-ACSSSPSKHCG-OH, Cyclic; TD-1)

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

Cat. No. 616365 **5 mg** **€ 172**

Ref.: Chen, Y., et al. 2006. *Nat. Biotechnol.* **24,** 455.

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