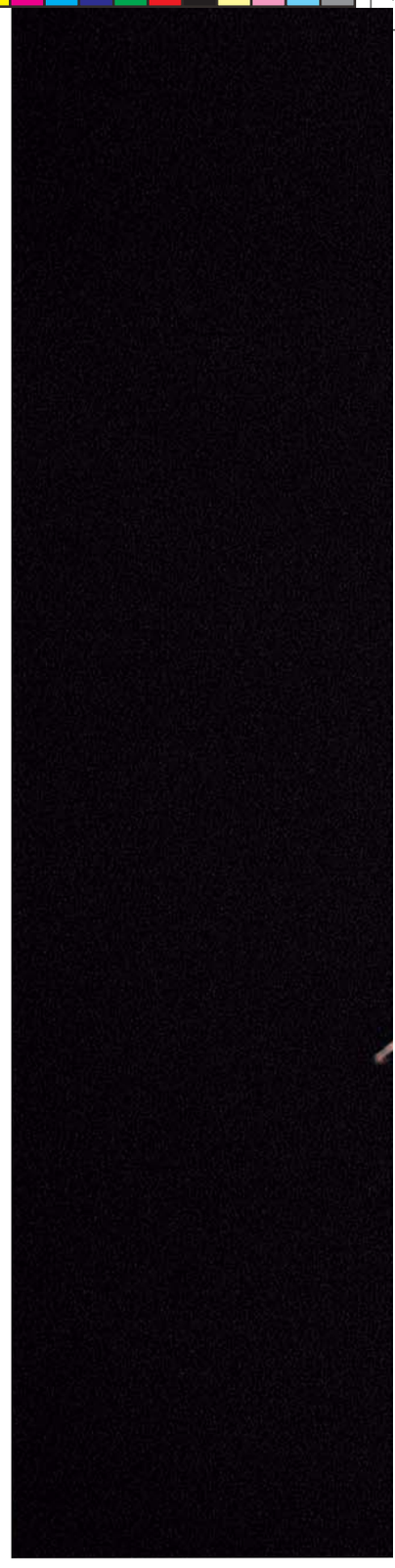

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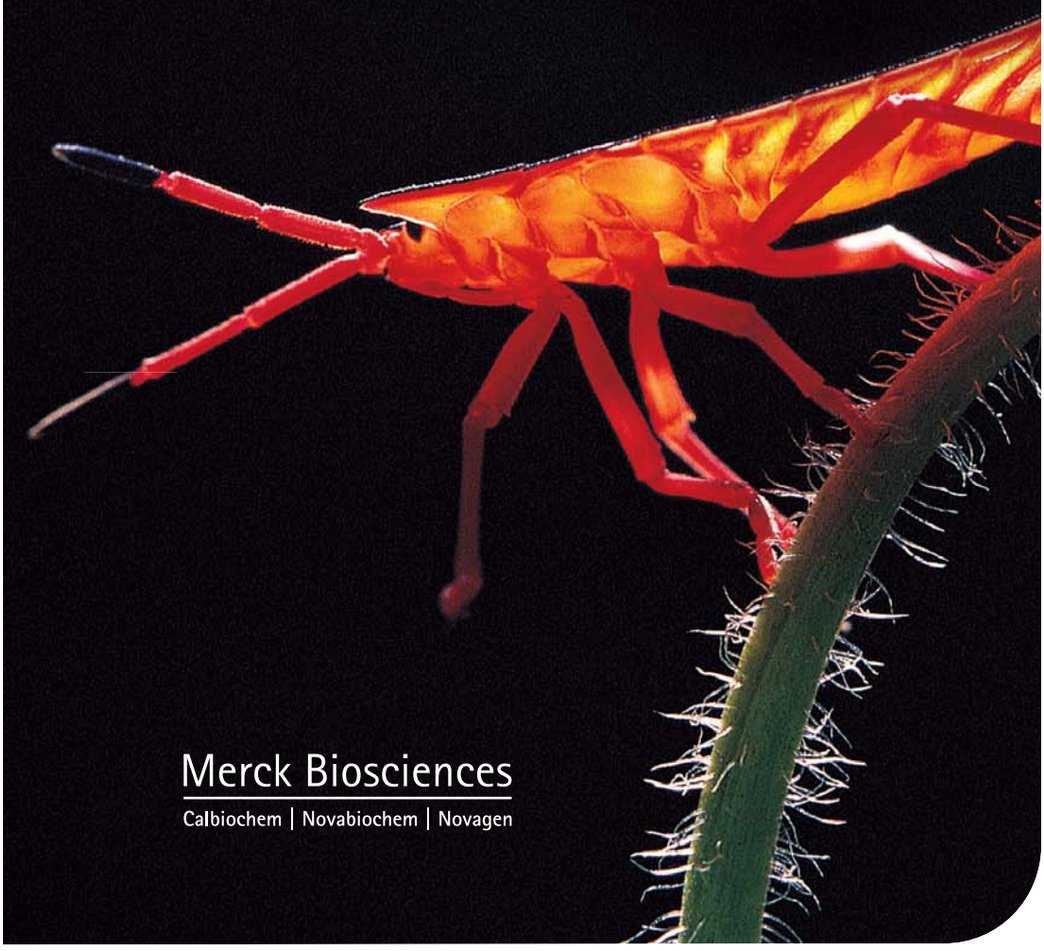
Biologics

Tubulin Polymerization and Depolymerization: Exploiting the Dynamic Instability of Microtubules



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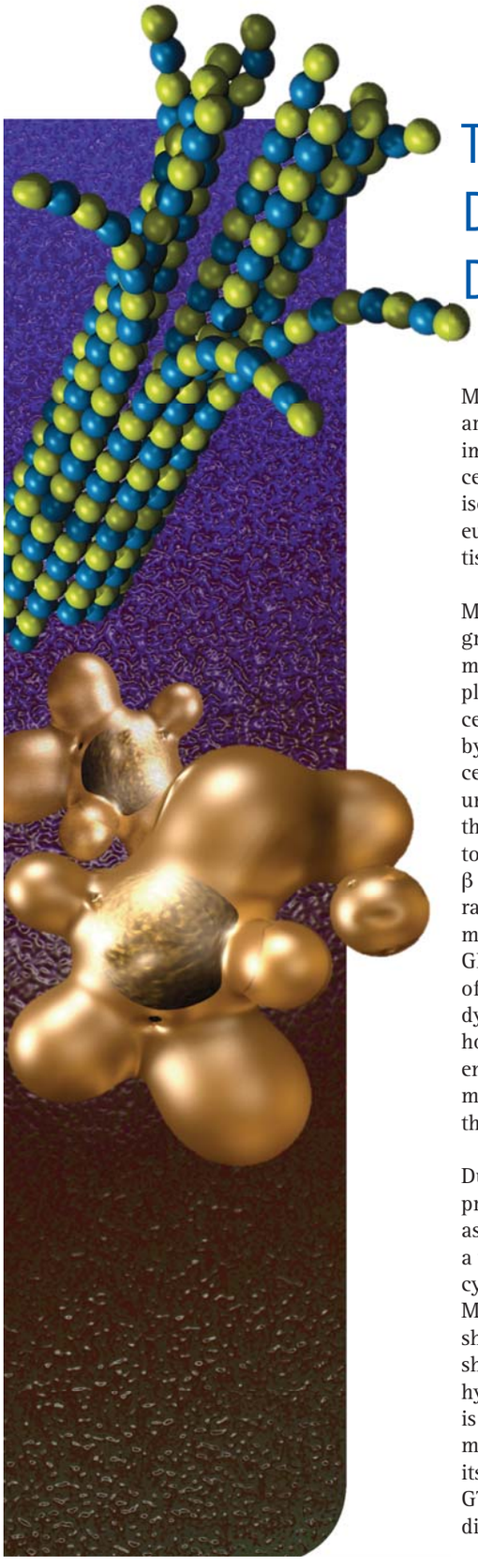

Tubulin Polymerization and Depolymerization: Exploiting the Dynamic Instability of Microtubules

Microtubules (MTs), rigid and hollow cylindrical structures of about 25 nm diameter, are composed of α-and β-tubulin dimers. They determine cell shape and play an important role in diverse processes such as cell division, cell motility and migration, cellular transport, and signal transduction. Both α and β tubulins exist in several isotypic forms and can undergo several post-translational modifications. In higher eukaryotes at least 14 tubulin isotypes have been reported that are expressed in a tissue-specific manner.

MTs are polar structures with two distinct ends, a fast growing "plus" end and a slow growing "minus" end. In most cells, MTs are organized into a single array with their minus ends associated with a MT organizing center located near the nucleus, and their plus ends located toward the cell's periphery near the plasma membrane. This gives the cell a defined polarity based on the inherent polarity of MTs. This polarity is utilized by the MT-associated motor proteins that move "cargo" to the minus or plus ends of cellular MTs. Tubulin dimers constantly polymerize and depolymerize, and MTs can undergo rapid cycles of assembly and disassembly. The first stage of MT formation, the nucleation phase, is slow. In the presence of Mg^{2+} and GTP, α and β tubulins join together in an end-to-end manner to form protofilaments with alternating α and β subunits. The second phase, also known as the elongation phase, proceeds rather rapidly. For tubulin heterodimerization and association of tubulins to form MTs, GTP must be bound to both α and β subunits. GTP bound to β-tubulin is hydrolyzed to GDP during or immediately after polymerization. This weakens the binding affinity of tubulin for adjacent molecules and favors depolymerization that contributes to the dynamic behavior of MTs. Heterodimers can add or dissociate at either end of a MT; however, there is greater tendency for addition to occur at the faster growing plus end where β-tubulin is exposed. MTs also undergo "treadmilling," in which tubulin molecules bound to GDP are continually lost from the minus end and are replaced by the addition of GTP-bound tubulin molecules to the plus end of the same MT.

During the formation of MTs, the alternating elongation and shortening cycles provide dynamic instability that is critical for directing MTs towards target sites, such as kinetochores, focal adhesions, and migrating membranes. Dynamic instability, a tightly regulated phenomenon, is particularly critical for the remodeling of the cytoskeleton during mitosis. It is characterized by four important variables: the rate of MT growth, the rate of shortening, the frequency of transition from the growth state to shortening, and the frequency of transition from shortening to growth. The growth and shortening of a MT depend upon the rate of tubulin addition relative to the rate of GTP hydrolysis. Tubulin-bound GTP is hydrolyzed to tubulin-GDP + P_i and tubulin-GTP is added to the plus end almost simultaneously. However, when GTP-bound tubulin molecules are added more rapidly than GTP is hydrolyzed, the MT retains a GTP cap at its plus end and the growth continues. When the rate of polymerization declines, the GTP bound to tubulin at the plus end is hydrolyzed to GDP and the GDP-bound tubulin dissociates, resulting in rapid depolymerization and shrinkage of MT.

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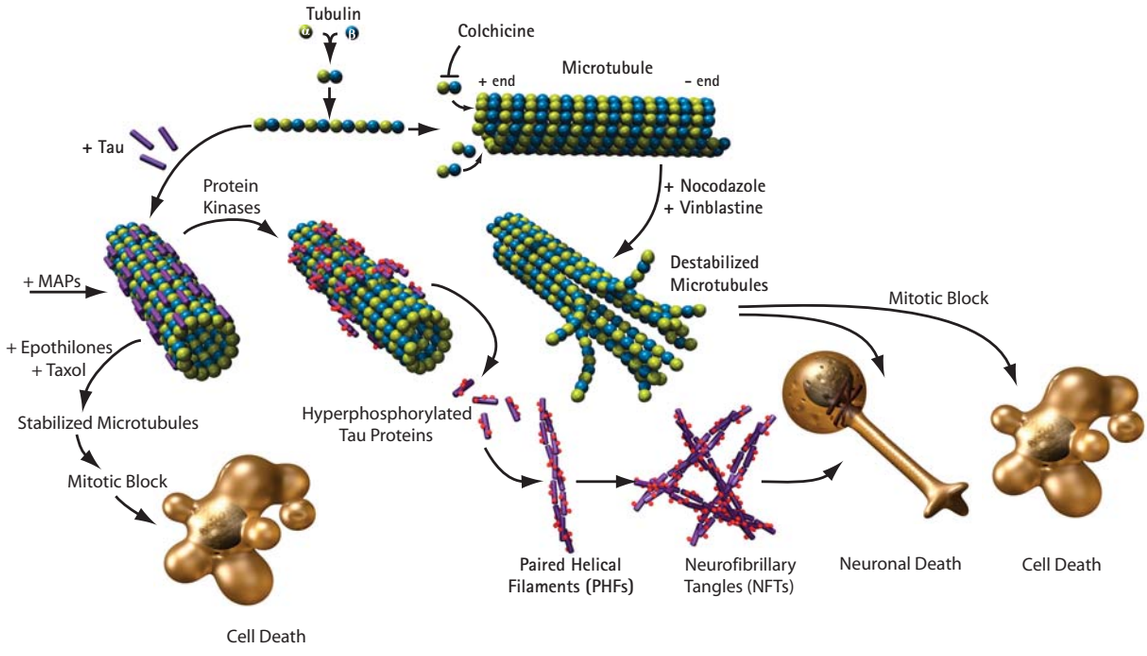

The inherent dynamic instability of MTs can be modified by the interactions with MT-associated proteins (MAPs) and MT-regulatory proteins. For example, MAPs can bind to MTs and increase their stability, while other proteins act to disassemble MTs, by increasing the rate of tubulin depolymerization. The best-characterized MAPs are MAP-1, MAP-2, and tau proteins. The activity of MAPs is tightly regulated by their phosphorylation state and altered phosphorylation state of MAPs has been positively linked to the pathogenesis of Alzheimer's disease. Growth factor signals can activate protein kinases that catalyze phosphorylation of tubulin-binding domains of MAPs and allow them to detach from MTs. XMAP215, a highly conserved MAP of 215 kDa, plays an important role in controlling MT dynamics during the cell cycle. It stabilizes the plus ends of MTs, promoting growth at the plus end and preventing catastrophic shrinkage. At the onset of mitosis, higher phosphorylation of XMAP215 results in increased MT instability, leading to disassembly. During the end of mitosis, protein phosphatase activity predominates as the MT array of interphase is re-established.

Given their essential role in the formation of the mitotic spindle during cell division, MTs have been very attractive targets for cancer chemotherapy. Anti-mitotic agents that can selectively disrupt MT dynamics, either by targeting a specific tubulin isotype or a particular stage of cell division have great potential value as chemotherapeutic agents. These agents exploit the difference in MT dynamics between rapidly dividing cancerous cells and normal cell populations. For example, drugs such as colchicine and colcemid bind tubulin and inhibit MT polymerization, thus blocking mitosis. On the other hand, agents such as taxol stabilize MTs and prevent cell division.

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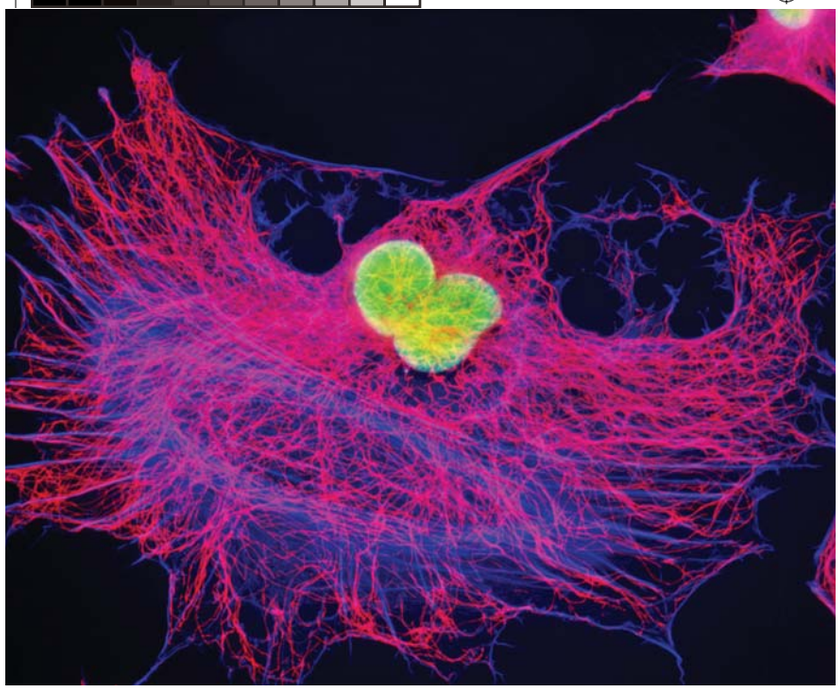


Photo courtesy of Michael W. Davidson, The Florida State University.

Anti-α-Tubulin, Chicken (Mouse Monoclonal)

Immunogen: Native chick brain microtubules
Form: Liquid, purified
Reacts with: Chicken, Gerbil, Human, Mouse, Rat
Positive Control: Any cell line
Application: Immunofluorescence, Western Blot
Comments: Tubulin (~60 kDa) is found in all cells. May be used as a positive control. Use fresh samples for immunoblotting.

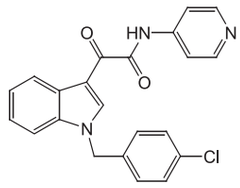
Clone: DMA1A Isotype: IgG_1

Cat. No. CP06 100 µg € 274

A monolayer culture of Swiss mouse embryo cells (illustrated left) was immunofluorescently labeled with mouse anti-α-tubulin primary antibodies, and then subsequently treated with a mixture of secondary antibodies conjugated to Alexa Fluor® 568 in a mixture containing phalloidin conjugated to Alexa Fluor® 350. The cell nuclei were counterstained with SYTOX® Green. Images were recorded in grayscale with a QImaging Retiga Fast-EXi camera system coupled to an Olympus BX-51 microscope equipped with bandpass emission fluorescence filter optical blocks provided by Omega Filters. During the processing stage, individual image channels were pseudocolored with RGB values corresponding to each of the fluorophore emission spectral profiles.

NEW! Tubulin Polymerization Inhibitors

D-24851 (N-(Pyridin-4-yl)-[1-(4-chlorobenzyl)-indol-3-yl]-glyoxyl Amide)



A cell-permeable, potent microtubule-destabilizing agent. Binds directly to tubulin and inhibits polymerization (IC_{50} = 300 nM). Blocks cell cycle at G2/M phase and shows efficacy toward multidrug-resistant tumor cells. *Purity: ≥98% by HPLC.* M.W. 398.8.

Cat. No. 251405 1 mg € 167

Ref.: Bacher, G., et al. 2001. *Cancer Res.* **61**, 392.

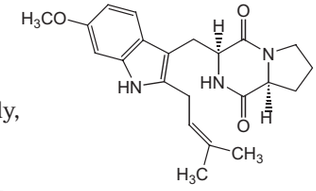
Stathmin, Human, Recombinant, *E. coli*

A highly conserved cytosolic phosphoprotein that acts as a tubulin-sequestering protein via formation of a T2S tight ternary complex. Interferes with the dynamic instability of microtubules *in vitro* and *in vivo*. *In vitro*, it either promotes rapid depolymerization of microtubules or prevents microtubule assembly in polymerization inhibition assays. *Purity: ≥95% by SDS-PAGE.* M.W. 17172.0

Cat. No. 569390 100 µg € 352

Ref.: Curmi, P.A., et al. 1997. *J. Biol. Chem.* **272**, 25029; Jourdain, L., et al. 1997. *Biochemistry* **36**, 10817; Curmi, P.A., et al. 1994. *Biochem J.* **300,** 331.

Tryprostatin A, *Aspergillus fumigatus*

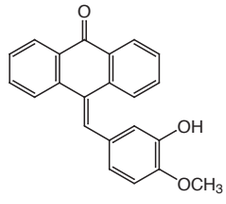


A specific inhibitor of microtubule-associated protein (MAP)-dependent microtubule assembly, which, through the disruption of the microtubule spindles, inhibits cell cycle progression at the M phase. *Purity: ≥95% by HPLC.* M.W. 395.5.

Cat. No. 649305 500 µg € 221

Ref.: Zhao, S., et al. 2002. *J. Med. Chem.* **45**, 1559; Usui, T., et al. 1998. *Biochem. J.* **333**, 543.

Tubulin Polymerization Inhibitor (10-[(3-Hydroxy-4-methoxybenzylidene)]-9(10H)-anthracenone)



A cell-permeable antimicrotubule agent with antitumor properties (IC_{50} = 20 and 50 nM in inhibiting growth of K562 and SKOV3 cells, respectively). Does not function as a substrate for Pgp-170 and exhibits cytotoxicity even towards tumor cell lines with various MDR phenotypes. Shown to interact with tubulin at the colchicine, but not the vinblastine, binding site. *Purity: ≥95% by HPLC.* M.W. 328.4.

Cat. No. 654160 5 mg € 100

Ref.: Prinz, H., et al. 2003. *J. Med. Chem.* **46**, 3382.

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Also available...

trans-HR22C16

A cell-permeable, potent blocker of cell division that targets the motor function of the mitotic kinesin Eg5 (IC_{50} = 800 nM). *Purity: ≥97% by HPLC*. M.W. 389.5.

Cat. No. 385861 **1 mg** **€ 82**

Ref.: Hotha, S., et al. 2003. *Angew. Chem. Int. Ed.* **42**, 2379.

(±)-Blebbistatin

A cell-permeable, selective, potent, and reversible inhibitor of nonmuscle myosin II. Inhibits the ATPase and gliding motility of human platelets (≤100 □M) without affecting myosin light chain kinase (MLCK) activity. Has been shown to block cell blebbing and rapidly disrupt directed migration and cytokinesis in vertebrate cells. Does not disrupt mitosis or affect contractile ring assembly. *Purity: ≥97% by HPLC*. M.W. 292.3.

Cat. No. 203390 **5 mg** **€ 171**

Ref.: Kovacs, M., et al. 2004. *J. Biol. Chem.* **279**, 35557; Straight, A.F., et al. 2003. *Science* **299**, 1743.

(–)-Blebbistatin

The active enantiomer of (±)-Blebbistatin (Cat. No. 203390) that accounts for the inhibitory activity towards ATPase (IC_{50} ~ 2 µM) and myosin II-dependent cellular processes. *Purity: ≥98% by Chiral HPLC*. M.W. 292.3.

Cat. No. 203391 **1 mg** **€ 138**

(+)-Blebbistatin

The inactive enantiomer of (±)-Blebbistatin (Cat. No. 203390). Useful as a negative control for the active enantiomer (Cat. No. 203391). *Purity: ≥98% by Chiral HPLC*. M.W. 292.3.

Cat. No. 203392 **1 mg** **€ 112**

Epothilone A, Synthetic

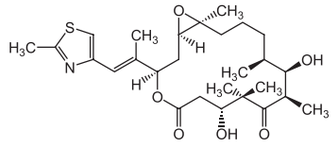
A sixteen-membered macrolide natural product that exhibits all the biological effects of Paclitaxel (Cat. No. 580555). Exhibits kinetics similar to paclitaxel in inducing tubulin polymerization *in vitro* and in producing enhanced microtubule stability and bundling in cultured cells. However, in contrast to paclitaxel, EpoA retains a much greater toxicity against P-glycoprotein-expressing multidrug resistant (MDR) cells (IC_{50} = 20 nM for MDR CCRF-CEM/VBL_{100} cells). *Purity: ≥95% by NMR*. M.W. 493.7. *Not available for sale in Germany.*

Cat. No. 325000 **25 µg** **€ 269**

Ref.: Chou, T.-C., et al. 1998. *Proc. Natl. Acad. Sci. USA* **95**, 9642; Kowalski, R.J., et al. 1997. *J. Biol. Chem.* **272**, 2534; Bollag, D.M., et al. 1995. *Cancer Res.* **55**, 2325.

Epothilone B, Synthetic

A structural analog of Epothilone A (Cat. No. 325000) with similar biological properties. However, EpoB is about 10-fold more potent than EpoA against P-glycoprotein-expressing multidrug resistant (MDR) cells (IC_{50} = 2 nM for MDR CCRF-CEM/VBL_{100} cells). *Purity: ≥95% by NMR*. M.W. 507.7. *Not available for sale in Germany.*

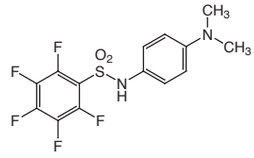


Cat. No. 325001 **10 µg** **€ 162**

Ref.: Giannakakou, P., et al. 2000. *Proc. Natl. Acad. Sci. USA* **97**, 2904; Chou, T.-C., et al. 1998. *Proc. Natl. Acad. Sci. USA* **95**, 9642; Kowalski, R.J., et al. 1997. *J. Biol. Chem.* **272**, 2534; Bollag, D.M., et al. 1995. *Cancer Res.* **55**, 2325.

T113242 [(4-N, N'-Dimethylanilino)-penta-fluorosulfonamide]

A cell-permeable inducer of microtubule depolymerization that irreversibly modifies β-tubulin. *Purity: ≥95% by HPLC*.

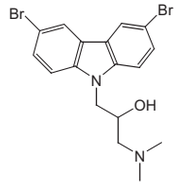


Cat. No. 575307 **10 mg** **€ 124**

Ref.: Ziegelbauer, J., et al. 2004. *Proc. Natl. Acad. Sci. USA* **101**, 458. Ziegelbauer, J., et al. 2001. *Mol. Cell* **8**, 339.

Wiskostatin

A cell-permeable, selective blocker of actin filament assembly. Acts as a selective, reversible inhibitor of N-WASP (neural Wiskott Aldrich syndrome protein), a signal integrating protein. Appears to bind to N-WASP, stabilize the autoinhibited conformation and prevent the activation of Arp2/3 (actin-related protein 2/3) complex. *Purity: ≥95% by HPLC*.



Cat. No. 681525 **1 mg** **€ 102**
5 mg **€ 355**

Ref.: Peterson, J.R., et al. 2004. *Nat. Struct. Mol. Biol.* **11**, 747; Peterson, J.R., and Mitchison, T.J. 2002. *Chem. Biol.* **9**, 1275.

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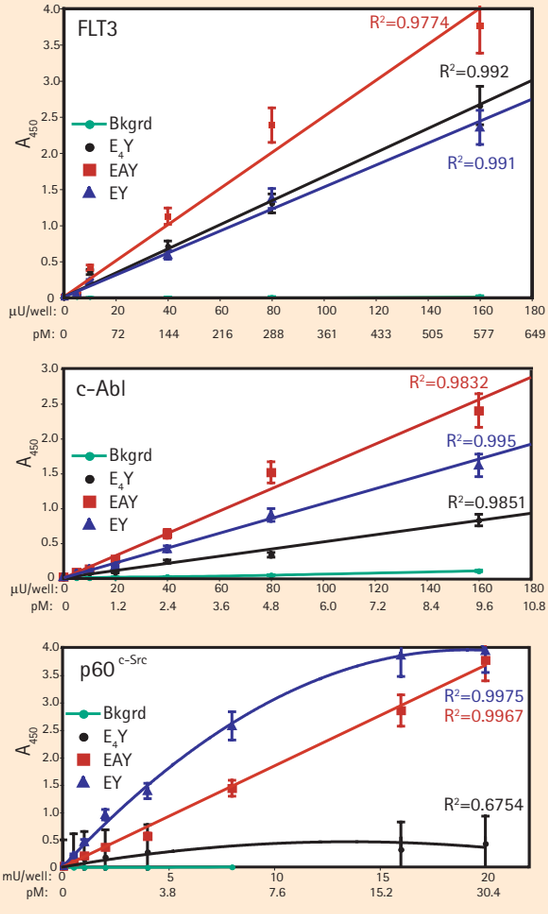
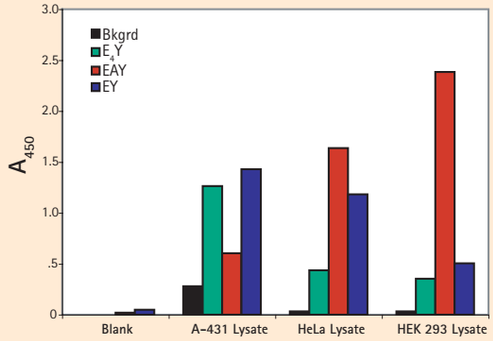


PTK activity of purified PTKs

Purified FLT3, c-Abl, and Src PTKs were diluted in reaction buffer and added to each well of the K-LISA™ PTK Screening plate. The plate was incubated at 30°C for 30 min. To stop the reaction, 250 µM EDTA was added and the plate was washed three times with PBS supplemented with 0.05% TWEEN®-20 (PBS-T). Anti-Phosphotyrosine (PY20) (Mouse) Peroxidase Conjugate was diluted to 1:2000 in PBS-T supplemented with 1% BSA, and added at 100 µl per well. After incubating for 30 min at room temperature, the plate was washed as above, and 100 µl TMB (soluble) per well was added. The plate was incubated at room temperature until color development. The reaction was stopped by adding 100 µl 0.5 N H_2SO_4 to each well and the absorbance was read at 450 nm. All experiments were performed in triplicate.



PTK activity in human cell lysates, determined with the K-LISA™ PTK Screening Kit

The K-LISA™ PTK Screening Kit was used to measure PTK activity in the indicated cell lysates (5 µg/well total protein) prepared using PhosphoSafe™ Extraction Buffer (Cat. No. 71296). Values shown are derived by subtraction of the PBS blank signal (typically 0.05–0.07 absorbance units at 450 nm) from the sample signal.

Calcineurin Autoinhibitory Peptide, Cell-Permeable [11R-CaN-AID]

Cat. No. 207001 **1 mg** **€ 194**

Ref.: Terada, H., et al. 2003. *J. Neurochem.* **87**, 1145.

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Suitable for selective capture of phosphorylated peptides derived from cleaved or digested protein samples. The magnetic particle based kit allows for the convenient enrichment of phosphopeptides ready for mass spectrometric analysis in 30 minutes. Each kit is sufficient for up to 100 isolations of 2.5 nanomoles phosphopeptide.

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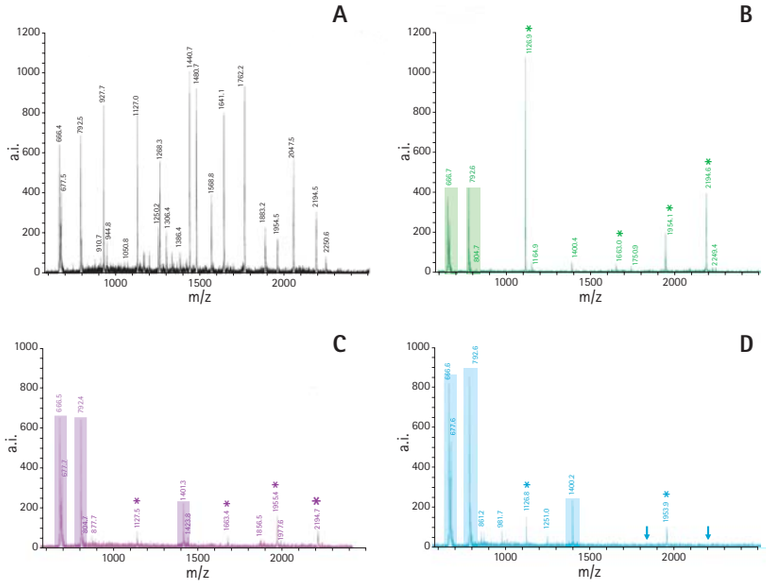


Figure: MALDI-MS spectra of various phosphopeptide using different isolation methods

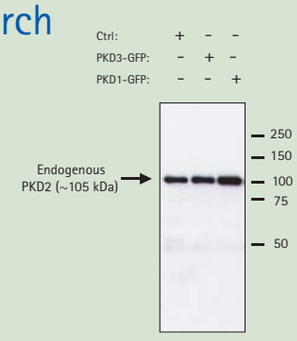
BSA, α-Casein, and Histone type IIB1 were mixed, digested with trypsin, and supplemented with a serine-phosphopeptide and a tyrosine-phosphopeptide. Analysis was performed on a MALDI-TOF instrument in linear mode, positive ion selection, and 4-hydroxy-alpha-cyanocinnamic acid as the matrix. Resulting spectra show phosphopeptide ions, identified by asterisks (*), and contaminating peptides, identified by shading. Panel A shows an unprocessed sample. Panel B shows a sample processed using the ProteoExtract® Phosphopeptide Capture Kit, which detected four phosphopeptides (*). Panel C shows a sample processed using a kit from supplier X, which also detected four phosphopeptides, but at reduced signal intensity and with contaminating non-phosphorylated peptides. Panel D shows a sample processed using a kit from supplier Y that detects only two of the phosphopeptides (positions of the missing phosphopeptide ions are marked by arrows); the most intense peaks represent contaminating non-phosphorylated peptides.

NEW! Antibodies for Protein Kinase Research

Anti-PKD2, Human (Rabbit)

Immunoaffinity-purified. Immunogen used was a synthetic peptide corresponding to region near the C-terminus of PKD2. Detects the ~105 kDa PKD2. Reacts with human, mouse, and rat. Suitable for immunoblotting and immunoprecipitation. Supplied at 1 mg/ml.

Cat. No. ST1042 **50 µg** **€ 190**



HEK293 cell lysate (30 µg protein/lane) was subjected to Western blot analysis using ST1042 (1:1000). Cells transfected with PKD1 or PKD3 fusion protein (136 kDa) were used as negative controls.

Western blotting

Anti-p70S6 Kinase, Human (Rabbit)

Immunoaffinity-purified antibody raised against a synthetic peptide corresponding to the C-terminus of p70S6 kinase. Detects the ~70 kDa p70S6 kinase. Reacts with human, mouse, and rat. Suitable for immunoblotting. Supplied at 1 mg/ml.

Western blot of rat L6 myoblast lysate using ST1046 at 1:10,000 dilution.

Cat. No. ST1046 **100 µg** **€ 361**

Anti-RKIP, Rat (Rabbit)

Undiluted serum. Immunogen used was a full-length recombinant GST-RKIP fusion protein. Detects the ~23 kDa Raf Kinase Inhibitory Protein (RKIP). Suitable for immunoblotting and immunocytochemistry.

ST1041 was used at 1:1000 dilution.

Cat. No. ST1041 **50 µl** **€ 165**

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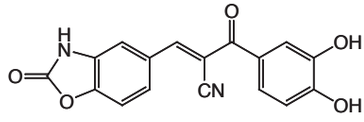
NEW! Protein Kinase Inhibitors

AGL 2263

A cell-permeable benzoxazolone-containing bioisostere of tyrphostin AG 538 (Cat. No. 658403) that acts as a potent, substrate-competitive, but not ATP-competitive, inhibitor of insulin receptor (IR) and insulin-like growth factor-1 receptor (IGF-1R) (IC_{50} = 400 and 430 nM, respectively). Inhibits Src and Akt/PKB only at much higher concentrations (IC_{50} = 2.2 and 55 µM, respectively). *Purity: ≥97% by HPLC.* M.W. 322.3.

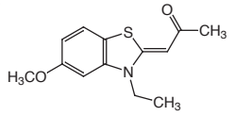


Cat. No. 121850 **5 mg** **€ 181**

Ref.: Blum, G., et al. 2003. *J. Biol. Chem.* **278**, 40442.

Cdc2-Like Kinase Inhibitor, TG003

A cell-permeable, potent, specific, reversible, and ATP-competitive inhibitor of Clk-family of kinases (Ki = 10 nM for mClk1/Sty; IC50 = 15 nM, 20 nM, 200 nM, and > 10 µM for mClk4, mClk1, mClk2, and mClk3, respectively). *Purity: ≥98% by HPLC.* M.W. 249.3.



Cat. No. 219479 **5 mg** **€ 98**

Ref.: Muraki, M., et al. 2004. *J. Biol. Chem.* **279**, 24246.

Cdk4 Inhibitor

A cell-permeable, potent, selective, and ATP-competitive inhibitor of Cdk4/D1 (IC50 = 76 nM). Inhibits the activity of other Cdk's only at much higher concentrations (IC50 = 520 nM and 2.1 µM for Cdk2/E and Cdk1/B, respectively). *Purity: ≥95% by HPLC.* M.W. 404.2.

Cat. No. 219476 **1 mg** **€ 100**

Ref.: Zhu, G., et al. 2003. *J. Med. Chem.* **46**, 2027.

EGFR/ErbB-2 Inhibitor [4-(4-Benzyloxyanilino)-6,7-dimethoxyquinazoline]

A cell-permeable, potent, reversible, and ATP-competitive inhibitor of EGFR and c-erbB-2 (IC_{50} = 20 nM and 79 nM, respectively). Inhibits proliferation of tumor cells overexpressing EGFR or c-erbB-2 (IC_{50} ~ 1.2 - 2.5 µM). *Purity: ≥97% by HPLC.* M.W. 387.4.

Cat. No. 324673 **1 mg** **€ 98**

Ref.: Cockerill, S., et al. 2001. *Bioorg. Med. Chem. Lett.* **11**, 1401.

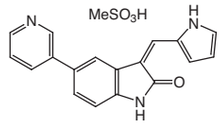
JAK3 Inhibitor VI

A cell-permeable, potent inhibitor of JAK3 (IC_{50} = 27 nM). Binds to the enzyme active site and prevents IL-2-induced cellular phosphorylation of JAK3 and STAT5. *Purity: ≥98% by HPLC.* M.W. 383.4.

Cat. No. 420126 **5 mg** **€ 138**

Ref.: Adams, C., et al. 2003. *Bioorg. Med. Chem. Lett.* **13**, 3105.

JNK Inhibitor IV (D)-Form, Cell-Permeable[(D)-HIV-TAT_{48-57}-PP-JBD_{20}]



An all-D *retroinverso* version of (L)-JNKI1 peptide (Cat. No. 420116) that readily crosses blood brain barrier and competitively blocks access of JNK to many of its targets. Although ~15-fold less potent than (L)-JNKI1, it is more protease-resistant and offers inhibition of MAPK-JNK signaling pathway for extended periods of time both *in vitro* and *in vivo*. *Purity: ≥97% by HPLC.*

Cat. No. 420117 **250 µg** **€ 274**

Ref.: Dai, Y., et al. 2003. *Oncogene* **22**, 7108; Borsello, T., et al. 2003. *Nat. Med.* **9**, 1180; Desbiens, K.M., et al. 2003. *Biochem. J.* **372**, 631; Minogue, A.M., et al. 2003. *J. Biol. Chem.* **278**, 27971.

Olomoucine II

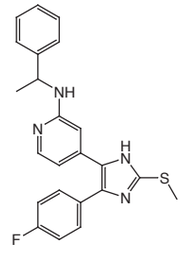
A cell-permeable, potent, ATP-competitive inhibitor of Cdk1/cyclin B (IC_{50} = 20 nM).

Cat. No. 495621 **5 mg** **€ 179**

Ref.: Krystof, V., et al. 2002. *Bioorg. Med. Chem. Lett.* **12**, 3283.

p38 MAP Kinase Inhibitor III

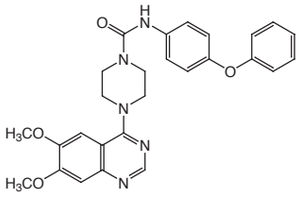
A cell-permeable, potent, selective, and ATP site-directed p38 MAP kinase inhibitor (IC_{50} = 380 nM for p38α). Compared with SB 203580 (Cat. No. 559389 and 559398), it exhibits reduced inhibitory activity against cytochrome P450-2D6 isoform and, therefore, is better suited for *in vivo* use. *Purity: ≥98% by HPLC.* M.W. 404.5.



Cat. No. 506121 **1 mg** **€ 144**

Ref.: Laufer, S.A., et al. 2003. *J. Med. Chem.* **46**, 3230.

PDGF Receptor Tyrosine Kinase Inhibitor III

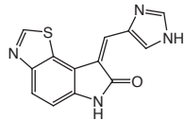


A cell-permeable piperazinyl-quinazoline carboxamide compound that acts as a potent, ATP-competitive, and selective inhibitor of PDGF receptor family of tyrosine kinases (IC_{50} = 50 nM for α-PDGFR; 80 nM for β-PDGFR; 50 nM for c-Kit; 230 nM for Flt3). *Purity: ≥97% by HPLC.* M.W. 485.5.

Cat. No. 521232 **1 mg** **€ 124**

Ref.: Matsuno. K., et al. 2003. *J. Med. Chem.* **46**, 4910; Matsuno, K., et al. 2003. *Bioorg. Med. Chem. Lett.* **13**, 3001; Matsuno. K., et al. 2002. *J. Med. Chem.* **45**, 4513. Matsuno, K., et al. 2002. *J. Med. Chem.* **45**, 3057.

PKR Inhibitor (RNA-dependent Protein Kinase Inhibitor)



An imidazolo-oxindole compound that acts as a potent, ATP-binding site directed inhibitor of PKR. Shown to effectively inhibit RNA-induced PKR autophosphorylation (IC_{50} = 210 nM) and rescue PKR-dependent translation block (IC_{50} = 100 nM). *Purity: ≥90% by HPLC.* M.W. 268.3.

Cat. No. 527450 **5 mg** **€ 112**

Ref.: Jammi, N.V., et al. 2003. *Biochem. Biophys. Res. Commun.* **308**, 50.

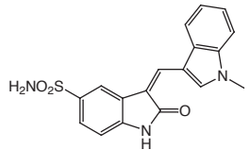
PKR Inhibitor, Negative Control [5-Chloro-3-(3,5-dichloro-4-hydroxybenzylidene)-1,3-dihydro-indol-2-one]

An oxindole compound that serves as a negative control for PKR Inhibitor (Cat. No. 527450) (IC_{50} > 100 µM). *Purity: ≥95% by HPLC.* M.W. 340.6.

Cat. No. 527455 **10 mg** **€ 112**

Ref.: Jammi, N.V., et al. 2003. *Biochem. Biophys. Res. Commun.* **308**, 50.

Syk Inhibitor



A cell-permeable, potent inhibitor of Syk (IC_{50} = 14 nM). *Purity: ≥98% by HPLC.* M.W. 353.4.

Cat. No. 574711 **5 mg** **€ 124**

Ref.: Lai, J.Y.Q., et al. 2003. *Bioorg. Med. Chem. Lett.* **13**, 3111.

TGF-β RI Kinase Inhibitor ([3-(Pyridin-2-yl)-4-(4-quinonyl)]-1H-pyrazole)

A cell-permeable, potent, selective, ATP-competitive inhibitor of TGF-β receptor I kinase (IC_{50} = 51 nM). Displays ~15-fold greater selectivity over p38α MAP kinase (IC_{50} = 740 nM). *Purity: ≥97% by HPLC.* M.W. 272.3.

Cat. No. 616451 **5 mg** **€ 124**

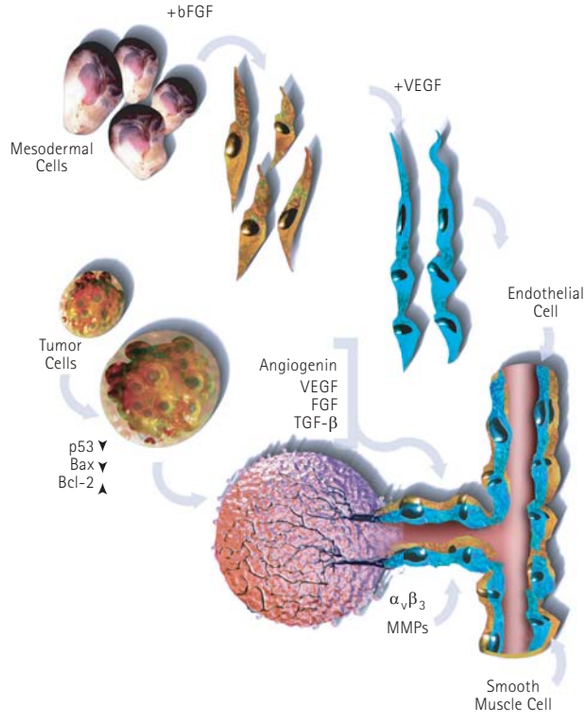
Ref.: Sawyer, J.S., et al. 2003. *J. Med. Chem.* **46**, 3953; Singh, J., et al. 2003. *Bioorg. Med. Chem. Lett.* **13**, 4355.

New! Tyrosine Phosphatases

Product	Cat. No.	Comments	Size	Price €
Protein Tyrosine Phosphatase PRL-2, GST-Fusion, Human, Recombinant, *E. coli*	**539806**	The catalytic domain of human PRL-2 (amino acids 2-167) expressed with an N-terminal GST fusion. PRL-2 is a protein tyrosine phosphatase that may function as a regulator of geranylgeranyltransferase II. Suitable for the dephosphorylation of phosphotyrosine residues in substrate proteins.	20 µg	214
Protein Tyrosine Phosphatase PRL-3, GST-Fusion, Human, Recombinant, *E. coli*	**539807**	The catalytic domain of human PRL-3 (amino acids 2-173) expressed with an N-terminal GST fusion. PRL-3 is a protein tyrosine phosphatase that is overexpressed in liver metastasis and colorectal cancer. Suitable for the dephosphorylation of phosphotyrosine residues in substrate proteins.	20 µg	214
Protein Tyrosine Phosphatase SHP-2, GST-Fusion, Human, Recombinant, *E. coli*	**565855**	The catalytic domain of human SHP-2 (amino acids 224-529) expressed with an N-terminal GST fusion. SHP-2 is a regulator of the JAK2 signaling pathway and may also regulate Akt. Suitable for the dephosphorylation of phosphotyrosine residues in substrate proteins.	20 µg	215

Angiogenesis: A Therapeutic Target for Cancer Therapy

The study of signaling processes involved in vascular development is important not only for understanding embryogenesis but also for developing therapeutic modalities for either reactivating or inactivating angiogenic pathways in disease states. There is considerable interest in developing angiogenic inhibitors to block tumor growth and metastasis. Most tumors can remain 2 to 3 mm in size for years without any angiogenic activity. In this dormant stage, the rate of tumor cell proliferation is balanced by apoptosis of tumor cells. However, when they switch to the angiogenic phenotype they grow rapidly. The obligatory neovascularization is a rather uncommon process under normal conditions. Hence, angiogenesis has become a prominent target for therapeutic intervention in cancer patients. Anti-angiogenic agents are highly selective in their action and affect only the vasculature. They offer reduced toxicity and are not prone to multi-drug resistance. Several recent studies have suggested that interference with the function of the VEGFR2 (KDR; Kinase insert Domain containing Receptor) is of particular importance in blocking tumor-induced angiogenesis.



Inhibitor of VEGF Receptor Tyrosine Kinases

Product	Cat. No.	Comments	Size	Price €
Oxindole I	**499600**	A potent and selective inhibitor of tyrosine kinase activity of VEGFR (IC_{50} = 390 nM for Flk-1). Inhibits PDGFR tyrosine kinase and Cdk4/cyclin D1 activity at much higher concentrations (IC_{50} = 12 µM and 4.9 µM, respectively).	10 mg	77
SU1498	**572888**	A potent and selective inhibitor of Flk-1 kinase (IC_{50} = 700 nM) that also reduces the expression of *ets-1*, a transcription factor stimulated by VEGF. Exhibits weak inhibitory effect on the kinase activity of PDGFR (IC_{50} > 50 µM), EGFR (IC_{50} > 100 µM), and HER2 (IC_{50} > 100 µM).	5 mg	147
SU5614	**572632**	A potent and selective inhibitor of tyrosine kinase activity of VEGFR (Flk-1; IC_{50} = 1.2 µM) and PDGFR (IC_{50} = 2.9 µM). *Not available for sale in the USA.*	1 mg	150
VEGF Receptor 2 Kinase Inhibitor I	**676480**	A cell-permeable, highly selective inhibitor of VEGFR2 tyrosine kinase (IC_{50} = 70 nM). The inhibition is suggested to be competitive with respect to ATP.	1 mg	118
VEGF Receptor 2 Kinase Inhibitor II	**676485**	A cell-permeable inhibitor of VEGFR2 tyrosine kinase (IC_{50} = 70 nM for VEGFR2, 920 nM for PDGF-Rβ, 4.92 µM for $p60^{c\text{-}src}$, and 13.3 µM for FGF-R1). The inhibition is suggested to be competitive with respect to ATP.	1 mg	118
VEGF Receptor 2 Kinase Inhibitor III	**676487**	A cell-permeable, selective inhibitor of VEGFR2 and PDGF-R tyrosine kinases (IC_{50} = 1.04 µM and 20 µM in NIH 3T3 cells overexpressing Flk-1; K_m = 530 nM for ATP).	1 mg	140
VEGF Receptor 2 Kinase Inhibitor IV	**676489**	A potent, ATP-competitive inhibitor of VEGFR2 tyrosine kinase (IC_{50} = 19 nM). Displays ~2-fold greater selectivity for VEGFR-2 over PDGFRβ (IC_{50} = 34 nM) and 10-fold greater selectivity over VEGFR1 (Flt-1) and VEGFR3 (Flt-4; IC_{50} = 190 nM) kinase activities.	1 mg	89
VEGF Receptor Tyrosine Kinase Inhibitor	**676475**	A potent inhibitor of VEGFR2 tyrosine kinase activity (IC_{50} = 2.0 µM and 100 nM for Flt and KDR, respectively).	1 mg	103

Orders: Tel 0800 6931 000
Fax 0800 6236 100
Republic of Ireland 1800 409445

NEW! Matrix Metalloproteinase Assay Kits

MMP-13, Proenzyme, ELISA Kit

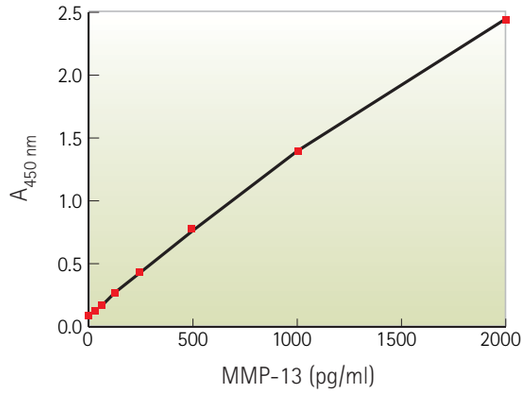
This MMP-13 ELISA Kit is designed to be a highly sensitive and specific assay for the quantitative determination of human MMP-13 proenzyme in serum, synovial fluid, and cell culture supernatants. A monoclonal antibody specific for the pro-MMP-13 is immobilized on a 96-well plate. The analyte is detected in two steps using a secondary biotin-labeled antibody and a highly polymerized streptavidin-peroxidase conjugate. The antibody does not cross-react with MMP-1, MMP-2, MMP-3, MMP-8, MMP-9, or the catalytic domains of MT-1, MT-2, MT-3, MT-4, or MT-5 MMP. Sensitivity: 4 pg/ml. Assay range: 4 – 100 pg/ml.

Cat. No. QIA126 **1 kit** **€ 654**

Active MMP-13 ELISA Kit

This kit is suitable for the detection of activated human MMP-13 in cell culture supernatants and body fluids such as serum and synovial fluid. Does not recognize MMP-1, MMP-2, MMP-3, MMP-8, MMP-9, or the latent form of MMP-13. Sensitivity: 7 pg/ml. Assay range: 32 – 2000 pg/ml.

Cat. No. QIA130 **1 kit** **€ 654**



A typical standard curve (prepared with assay buffer).

Also available...

NEW! Monoclonal antibody to MMP-13

Anti-MMP-13 (131-140), Human (Mouse)

Clone M31.387. Immunoaffinity-purified antibody suitable for the detection of the 54-60 kDa latent form of human MMP-13. Suitable for immunoblotting. Supplied at 100 µg/ml. *Not available for sale in Japan.*

Cat. No. IM87 **100 µg** **€ 351**

NEW! Inhibitors of Matrix Metalloproteinases

MMP-2/MMP-9 Inhibitor IV (SB-3CT)

A potent, selective, slow-binding and mechanism-based inhibitor of human gelatinases, MMP-2 (K_i = 13.9 nM), and MMP-9 (K_i = 600 nM). Binds directly to the catalytic zinc ion on MMP-2. *Purity: ≥ 95% by HPLC*. M.W. 306.4.

Cat. No. 444274 **500 µg** **€ 149**

Ref.: Kleinfeld, O., et al. 2001. *J. Biol. Chem.* **276**, 17125; Brown, S., et al. 2000. *J. Am. Chem. Soc.* **122**, 6799.

MMP-2 Inhibitor I (Oleoyl-N-hydroxylamide)

A potent inhibitor of MMP-2 that acts in a dose-dependent manner (K_i = 1.7 µM). *Purity: ≥98% by TLC*. M.W. 297.5.

Cat. No. 444244 **10 mg** **€ 82**

Ref.: Emonard, H., et al. 1999. *Ann. N.Y. Acad. Sci.* **878**, 647.

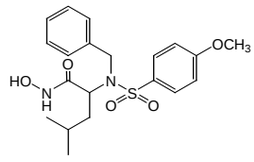
MMP-3 Inhibitor VII (3-[4-(4-Cyanophenyl)phenoxy]propanohydroxamic Acid)

A potent nonpeptide inhibitor of MMP-3 (stromelysin; IC_{50} = 25 nM against the catalytic domain). Purity: ≥95% by HPLC. M.W. 282.3.

Cat. No. 444280 **1 mg** **€ 120**

Ref.: Hajduk, P.J., et al. 1997. *J. Am. Chem. Soc.* **119**, 5818.

MMP-3 Inhibitor VIII (N-Hydroxy-2(R)-{[(4-methoxyphenyl)sulfonyl]-[benzylamino]}-4-methylpentanamide)

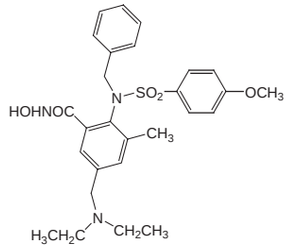


A cell-permeable, potent inhibitor of human MMP-3 (stromelysin; K_i = 23 nM) and murine macrophage metalloelastase (MME/MMP-12; IC_{50} = 13 nM). Binds to the MMP active site Zn^{2+}. *Purity: ≥97% by HPLC*. M.W. 406.5.

Cat. No. 444281 **5 mg** **€ 209**

Ref.: Jeng, A.Y., et al. 1998. *Bioorg. Med. Chem. Lett.* **8**, 897; MacPherson, L.J., et al. 1997. *J. Med. Chem.* **40**, 2525.

MMP-9 Inhibitor I



A potent and selective MMP-9 inhibitor (IC_{50} = 5 nM). Inhibits MMP-1 (IC_{50} = 1.05 µM) and MMP-13 (IC_{50} = 113 nM) only at much higher concentrations. *Purity: ≥95% by HPLC*. M.W. 511.6.

Cat. No. 444278 **500 µg** **€ 114**

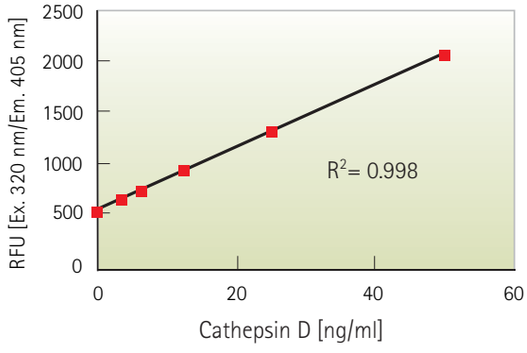
Ref.: Levin, J.I., et al. 2001. *Bioorg. Med. Chem. Lett.* **11**, 2189.

NEW! Cathepsin Assay Kits

InnoZyme™ Cathepsin D Immunocapture Activity Assay Kit, Fluorogenic

A selective, quantitative, and convenient fluorometric assay kit for determining cathepsin D activity. The assay uses a monoclonal anti-human cathepsin D antibody coated onto the wells of a 96-well plate to capture cathepsin D from standards, biological fluids, and culture media. The captured cathepsin D is detected using an internally quenched fluorescent peptide, Mca-GKPILFFRLK (DnP)-D-R-NH_2. Released Mca-GKPILF is quantified fluorometrically (Ex. max.: 328 nm, Em. max.: 393 nm.).

Cat. No. CBA002 **1 kit** **€ 539**

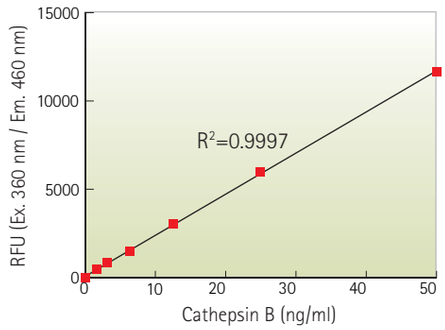


Representation of Cathepsin D activity in human cell lysates assayed with CBA002. Cell lysates were prepared with CytoBuster™ Protein Extraction Reagent, Cat. No. 71009.

InnoZyme™ Cathepsin B Activity Assay Kit, Fluorogenic

This fluorometric assay has been designed for the quantitative *in vitro* determination of cathepsin B activity. The test utilizes the ability of cathepsin B to digest the synthetic substrate Z-Arg-Arg-AMC. Released free AMC is determined fluorometrically (Ex. max: 360-380 nm; Em. max: 440-460 nm).

Cat. No. CBA001 **1 kit** **€ 392**



The activity of native cathepsin B (Cat. No. 219364) measured with Z-Arg-Arg AMC substrate in MES buffer, pH 6.0, in the presence of EDTA and cysteine. After incubation at 37°C for 30 minutes the free AMC was measured (Ex. max: 360 nm and Em. max: 460 nm).

NEW! InnoCyte™ ECM Cell Adhesion Assay Kits

The InnoCyte™ Cell Adhesion Assays are designed for the determination of the relative attachment of adherent cell lines to extracellular matrix proteins such as Human Fibronectin (Cat. No. CBA011), Human Vitronectin (Cat. No. CBA012), and Human Collagen IV (Cat. No. CBA013). Cells are seeded onto a coated substrate. After incubation followed by a brief wash step, attached cells are quantified with the green fluorescent dye calcein-AM. BSA-coated wells serve as a negative control, and poly-L-lysine-coated wells serve as a positive control for general attachment.

InnoCyte™ ECM Cell Adhesion Assay, Fibronectin

A convenient assay for the determination of the relative attachment of adherent cell lines to fibronectin. Cells are seeded onto the fibronectin plates followed by determination of relative cell attachment using a fluorescent dye (Ex. max: ~485 nm; Em. max: ~520 nm).

Cat. No. CBA011 **1 kit** **€ 181**

InnoCyte™ ECM Cell Adhesion Assay, Collagen Type IV

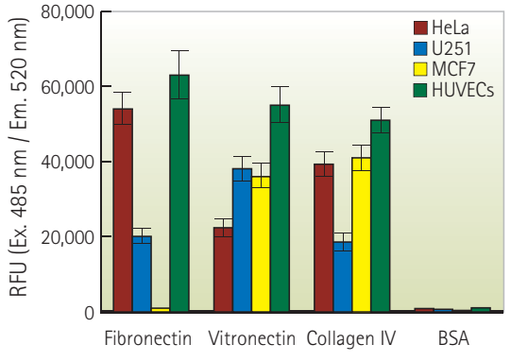
A convenient assay for the determination of the relative attachment of adherent cell lines to collagen type IV. Cells are seeded onto the collagen type IV coated plates followed by determination of relative cell attachment using a fluorescent dye (Ex. max: ~485 nm; Em. max: ~520 nm).

Cat. No. CBA013 **1 kit** **€ 218**

InnoCyte™ ECM Cell Adhesion Assay, Vitronectin

A convenient assay for the determination of the relative attachment of adherent cell lines to vitronectin. Cells are seeded onto the vitronectin plates followed by determination of relative cell attachment using a fluorescent dye (Ex. max: ~485 nm; Em. max: ~520 nm).

Cat. No. CBA012 **1 kit** **€ 281**



Approximately 25,000 cells were added to each well and allowed to attach for 1.5 hours at 37°C in 6% CO_2. Cells were washed gently with Dulbecco's PBS and labeled with calcein-AM for 1 hour at 37°C in 6% CO_2. The relative attachment of cells to poly-L-lysine was determined for HUVECs only and was lower than that of the displayed ECM proteins (data not shown).

Looking for Isozyme-specific Calpain Inhibitors?

Calpain Inhibitor IV (Z-LLY-FMK)
A potent, cell-permeable, and irreversible inhibitor of calpain-2 (k_2 = 28,900 $M^{-1}s^{-1}$). M.W. 557.7.

Cat. No. 208724 **1 mg** **€ 221**

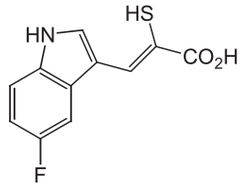
Ref.: Dutt, P., et al. 1998. *FEBS Lett. 436,* **367**; Angliker, H., et al. 1992. *J. Med. Chem.* **35**, 216.

Calpain Inhibitor VI [N-(4-Fluorophenylsulfonyl)-L-valyl-L-leucinal]
A potent, cell-permeable, reversible inhibitor of calpain. Exhibits about 10-fold greater selectivity for calpain-1 (IC_{50} = 7.5 nM) over calpain-2 (IC_{50} = 78 nM). Also acts as a potent inhibitor of cathepsins B (IC_{50} = 15 nM) and L (IC_{50} = 1.6 nM).

Cat. No. 208745 **1 mg** **€ 62**
5 mg **€ 222**

Ref.: Inoue, J., et al. 2003. *J. Med. Chem.* **46**, 868; Nath, R., et al. 2000. *Biochem. Biophys. Res. Commun.* **274**, 16; Fukiage, C., et al. 1997. *Biochim. Biophys. Acta* **1361**, 304.

PD151746 (3-(5-Fluoro-3-indolyl)-2-mercapto-(Z)-2-propenoic Acid)
A cell-permeable, non-peptidic highly selective calpain inhibitor that displays over 20-fold greater selectivity for calpain-1 (K_i = 260 nM) over calpain-2 (K_i = 5.33 □M).



Cat. No. 513024 **2 mg** **€ 203**

Ref.: Squier, M.K., et al. 1999. *J. Cell Physiol.* **178**, 311; Wang, K.K., et al. 1996. *Proc. Natl. Acad. Sci. USA* **93**, 6687.

Also available...

Calpain-1 Substrate, Fluorogenic [H-K(FAM)-EVY~GMMK(DABCYL)-OH]
An internally quenched fluorogenic substrate peptide derived from the calpain-1 cleavage site of α-spectrin. It is not recognized by trypsin or α-chymotrypsin and serves as a sensitive and specific substrate for calpain-1 (K_m = 4.6 µM; k_{cat} = 11 s^{-1}). Cleavage occurs between Tyr-Gly residues and results in enhanced fluorescence. *Purity: ≥95% by HPLC.* Ex. max.: ~490 nm, Em. max.: ~518 nm.

Cat. No. 208748 **2 mg** **€ 194**

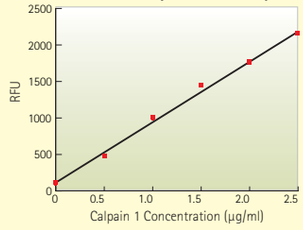
Ref.: Mittoo, S., et al. 2003. *Anal. Biochem.* **319**, 234.

NEW! Calpain Activity Assay Kit, Fluorogenic

A fluorometric assay kit designed to measure calpain activity in human cell lysates, plasma, and serum. Suitable for screening calpain inhibitors. The assay utilizes the unique ability of calpain to cleave AMC from Suc-LLVY-AMC in the presence of Ca^{2+} and TCEP. The kit includes highly purified native human calpain-1 (positive control), that should be included in every assay.

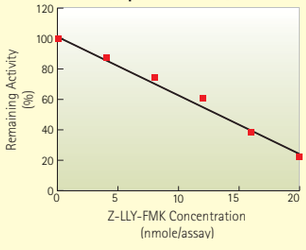
Cat. No. QIA120 **1 kit** **€ 429**

Human Calpain-1 Activity



Activity of native calpain-1 (Cat. No. 208713) was measured with 0.2 mM Suc-LLVY-AMC in imidazole buffer, pH 7.4, in the presence of $CaCl_2$ and the reducing agent TCEP. After incubation at room temperature the free AMC was measured (Ex. max: 360 nm; Em. max: 460 nm).

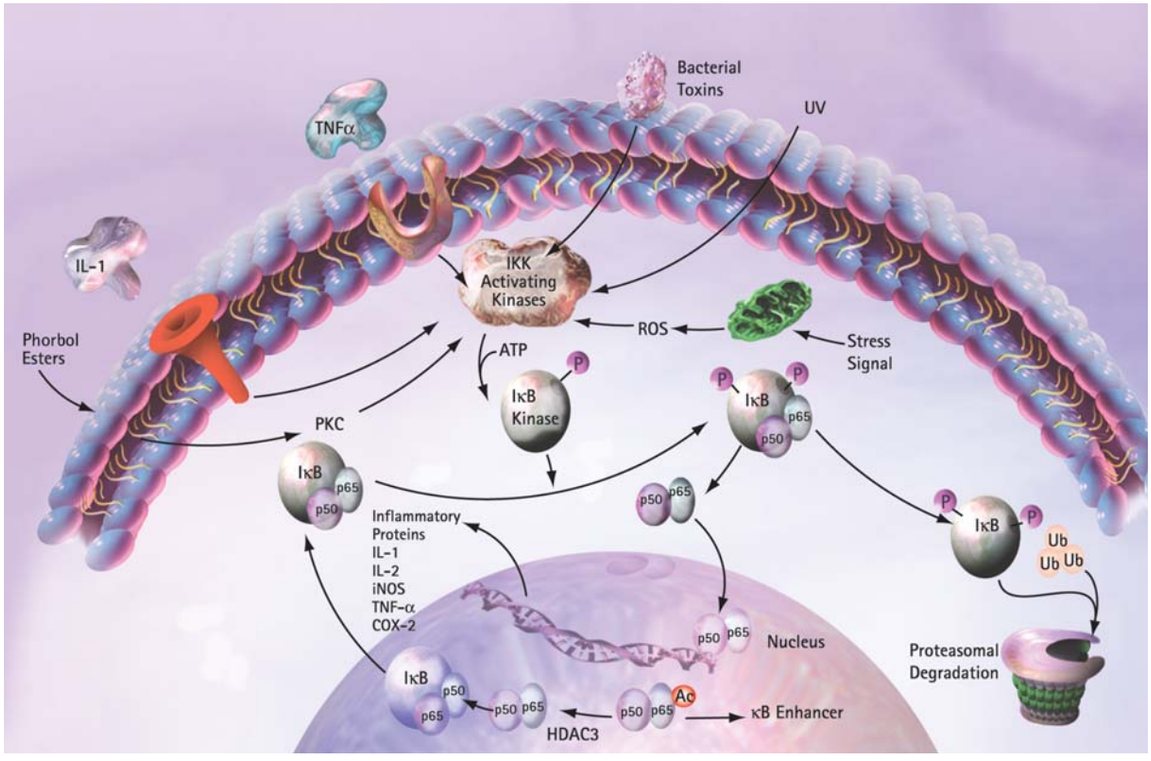
Calpain-1 Inhibition



Inhibition of human calpain-1 by Z-LLY-FMK. The remaining activity of the enzyme was assayed with 0.2 mM Suc-LLVY-AMC substrate at pH 7.4, in the presence of $CaCl_2$ and the reducing agent TCEP. The incubation was carried out at room temperature and the fluorescence was qualified (Ex. max: 360 nm; Em. max: 460 nm).

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

Nuclear factor-κB (NF-κB)/Rel transcription factors are known to play a pivotal role in inflammatory diseases. Aberrant regulation of NF-κB is also observed in autoimmune disorders and in different types of cancers. The signaling pathways leading to the regulation of NF-κB activity have become a focal point for drug discovery efforts. NF-κB is normally sequestered in the cytoplasm of nonstimulated cells and must be translocated into the nucleus to function. The subcellular location of NF-κB is controlled by a family of inhibitory proteins known as IκBs, which bind NF-κB and mask its nuclear localiziation signal thereby preventing its uptake into the nucleus.



The activation of NF-κB by the extracellular inducers depends on the phosphorylation and subsequent degradation of IκB proteins. Activation of NF-κB is achieved through the action of a family of serine/threonine kinases known as IκB kinase (IKK). The IKK contains two catalytic subunits (IKKα and IKKβ) and a regulatory/adapter protein NEMO (also known as IKKγ). The IKKα and IKKβ phosphorylate IκB proteins and the members of the NF-κB family. All IκB proteins contain two conserved serine residues within their N-terminal region, which are phosphorylated by IKK. IKKα and IKKβ share about 50% sequence homology and can interchangeably phosphorylate Ser^{32}/Ser^{36} of IκBα, and Ser^{19}/Ser^{23} of IκBβ . These phosphorylation events lead to the immediate polyubiquitination of IκB proteins and rapid degradation by the proteasomal pathway. Inhibitors of IKK have long been sought as specific regulators of NF-κB.

References: Karin, M., et al. 2004. *Nat. Rev. Drug Dis.* **3**, 17; Greten, F.R., and Karin, M. 2004. *Cancer Lett.* **206**, 193; Jones, W.K., et al. 2003. *Cardiovasc. Toxicol.* **3** 229; Richmond, A. 2002. *Nat. Rev. Immunol.* **2**, 664.

NEW! Anti-NF-κB (p65), Human (Mouse Monoclonal)

Protein-A purified. Immunogen used was a recombinant NF-κB (p65) comprised of ~175 amino acids from the C-terminus. Detects the ~65 kDa NF-κB. Clone No. 2A12A7. Suitable for ELISA, gel shift assay, and immunoblotting. Supplied at 1 mg/ml.

Cat. No. ST1047 **100 µl** **€ 269**

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NEW! IKK Inhibitors

IKK Inhibitor II, Wedelolactone

(7-Methoxy-5,11,12-trihydroxy-coumestan)

Active ingredient of the herbal medicine, *Eclipta alba*, that acts as a selective and irreversible inhibitor of IKKα and β kinase activity (IC_{50} < 10 µM). Inhibits NF-κB-mediated gene transcription in cells by blocking the phosphorylation and degradation of IκBα. *Purity: ≥98% by HPLC.* M.W. 314.3.

Cat. No. 401474 **1 mg** **€ 94**

Ref.: Kobori, M., et al. 2004. *Cell Death Differ.* **11**, 123. Li, C.C., et al. 2003. *J. Org. Chem.* **68**, 8500.

IKK-2 Inhibitor, SC-514

A cell-permeable, potent, reversible, ATP-competitive, and highly selective inhibitor of IKK-2 (IC_{50}s ~ 3 - 12 µM for IKK-2 homodimer, IKK-1/IKK-2 heterodimer, and IKK-2). Its specificity has been confirmed using a panel of 31 other kinases. *Purity: ≥98% by TLC.* M.W. 224.3.

Cat. No. 401479 **1 mg** **€ 94**

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

IKK Inhibitor III, BMS-345541

(Aminoethylamino-dimethylimidazo-quinoxaline, HCl)

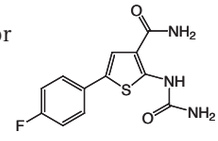
A cell-permeable, potent, selective, and allosteric site-binding inhibitor of IKK-2 (IC_{50} ~ 300 nM). Exhibits ~10-fold greater selectivity over IKK-1 (IC_{50} ~ 4.0 µM).

Cat. No. 401480 **1 mg** **€ 184**

Ref.: Townsend, R.M., et al. 2004. *Transplantation* **77**, 1090; MacMaster, J.F., et al. 2003. *Inflamm. Res.* **52**, 508; McIntyre, K.W., et al. 2003. *Arthritis Rheum.* **48**, 2652; Burke, J. R., et al. 2003. *J. Biol. Chem.* **278**, 1450.

IKK-2 Inhibitor IV

A cell-permeable, potent inhibitor of IKK-2 (IC_{50} = 18 nM).



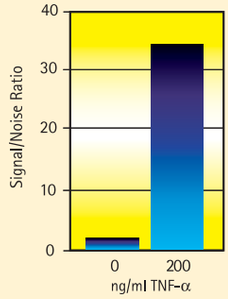
Cat. No. 401481 **500 µg** **€ 98**

Ref.: Podolin, P.L., et al. 2004. *J. Pharmacol. Exp. Ther.* **311**, In press; Karin, M., et al. 2004. *Nat. Rev. Drug Discov.* **3**, 17; Roshak, A.K., et al. 2002. *Inflamm. Res.* **51**, S4.

NoShift™ Transcription Factor Assay Kit

NEW! Non-radioactive, rapid, versatile, colorimetric detection system.

Measure the activation of DNA-binding proteins in less than five hours using the versatile 96-well NoShift™ Transcription Factor Assay Kit and NoShift™ NF-κB (p65) Reagents. The assay kit, an EMSA alternative, consists of the assay buffers, a streptavidin coated plate, and TMB substrate. The reagent kit includes the NF-κB consensus binding sequence (as a biotinylated oligionucleotide), an NF-κB antibody, and HRP detection antibody, as well as positive and negative controls.



After a 30-minute stimulation with 200 ng/ml TNF-α, nuclear extracts from the HeLa cells were prepared with NucBuster™kit (Cat. No. 71183-3). The nuclear extract was analyzed using NoShift NF-κB (p65) Reagents (Cat. No. 71518-3).

NoShift™ Transcription Factor Assay Kit

Cat. No. 71377-3 **1 kit** **€ 396**

NoShift™ NF-κB (p65) Reagents

Cat. No. 71518-3 **1 kit** **€ 222**

NEW! Antibodies for Proteasome/Ubiquitination Research

Product	Cat. No.	Comments	Size	Price €
Anti-CSN3, Human (Rabbit)	**ST1043**	Immunoaffinity-purified. Immunogen used was a synthetic peptide corresponding to a portion of CSN3 encoded within exon 10. Detects the ~40 kDa CSN3, a subunit of the COP9 signalosome complex. Supplied at 1 mg/ml. **IB**	100 µg	324
Ant-CSN4, Human (Rabbit)	**ST1044**	Immunoaffinity-purified. Immunogen used was a synthetic peptide corresponding to the C-terminus of CSN4. Detects the ~40 kDa CSN4 subunit of the COP9 signalosome complex. Supplied at 1 mg/ml. **IB**	100 µg	324
Anti-Jab1/CSN5, Human (Rabbit)	**ST1045**	Immunoaffinity-purified. Immunogen used was a synthetic peptide corresponding to the C-terminus of CSN5. Detects the ~33 kDa Jab1/CSN5, a subunit of the COP9 signalosome complex. Supplied at 1 mg/ml. **IB**	100 µg	324
Anti-Hip-2, Human and Mouse (Rabbit)	**NE1011**	Undiluted serum. Immunogen used was a synthetic peptide corresponding amino acid residues 1-12 of E2-25K/Hip-2. Detects the ~25 kDa E2-25K/Hip-2, an ubiquitin conjugating enzyme which has been reported to play a role in mediating amyloid-β neurotoxicity. Supplied at 1 mg/ml. **FS**, **IB**, **IP**, **PS**	50 µl	165
Anti-19S Regulator ATPase Subunit Rpt1, Human (Mouse Monoclonal)	**ST1058**	Undiluted serum. Immunogen used was recombinant human Rpt1 protein. Detects the ~48 kDa 19S Regulator ATPase Subunit Rpt1 protein, involved in the unfolding and translocation of substrates to the 20S proteasome's catalytic chamber. **IB**	100 µl	349
Anti-19S Regulator non-ATPase Subunit Rpn10, Human (Mouse Monoclonal)	**ST1060**	Purified. Immunogen used was recombinant human Rpt1 protein. Detects the ~45 kDa 19S regulator non-ATPase subunit Rpn10 protein, a non-ATPase subunit of the 19S regulatory complex of the 26S proteasome. **IB**, **IP**	100 µg	349
Anti-20S Proteasome α1, 2, 3, 5, 6, & 7-Subunits, Human (Mouse Monoclonal)	**ST1049**	Purified. Immunogen used was dinitrophenylated proteasomes. Reacts with six different α-type subunits. In ELISA the antibody reacts with the sequence ELISATVWSPQGRLHQVEYAMEA encompassing the prosbox I motif common to α-type. **ELISA**, **IB**	100 µg	349
Anti-20S Proteasome α3-Subunit, Human (Mouse Monoclonal)	**ST1050**	Purified. Immunogen used was human placental proteasomes. Detects the ~ 30 kDa 20S Proteasome α3-Subunit protein. Clone number: MCP257. **IB**	100 µg	349
Anti-20S Proteasome α5-Subunit, Human (Mouse Monoclonal)	**ST1051**	Purified. Immunogen used was dinitrophenylated human placental proteasomes. Detects the ~28 kDa 20S Proteasome α5-Subunit protein, involved in an ATP/ubiquitin-dependent non-lysosomal proteolytic pathway. Clone number: MCP196. **IB**	100 µg	349
Anti-PGP9.5 (Rabbit)	**NE1013**	Undiluted serum. Immunogen used was a synthetic peptide coresponding to amino acid residues 187-202 of PGP9.5. Detects the ~26 kDa PGP9.5, a ubiquitin hydrolase widely expressed in neuronal tissues and overexpressed in some cancers. **IB**, **PS**	50 µl	184

ELISA: Enzyme-linked immunosorbent assay; **IB:** immunoblotting; **IF:** immunofluorescence; **IP:** immunoprecipitation; **PS:** paraffin sections

NEW! Stable GTP Analogs: Adenylate Cyclase Inhibitors

MANT-GppNHp

A potent, competitive inhibitor of adenylyl cyclase (AC; K_i = 161 nM and 155 nM in forskolin/Mn^{2+}-stimulated AC in S49 cyc-membranes and insect cell membranes, respectively). A more lipophilic, fluorescent derivative of the GTP-hydrolysis-resistant GTP analog, GppNHp. Useful for investigating the interactions of low molecular weight GTP-binding proteins with their specific effector proteins. Supplied as a 5 mM solution in H_2O. *Purity: ≥90% by HPLC.* M.W. 958.9.

Cat. No. 444168 **50 µl** **€ 266**

Ref.: Gille, A., and Seifert, R. 2003. *J. Biol. Chem.* **278**, 12672; Diebold, B.A., and Bokoch, G.M. 2001. *Nat. Immunol.* **2**, 21; Ahmadian, M.R., et al. 1997. *Biochemistry* **36**, 4535; Neal, S.E., et al. 1990. *Proc. Natl. Acad. Sci. USA* **87**, 3562.

MANT-GTPγS

A potent, competitive inhibitor of adenylyl cyclase (AC; K_i = 53 nM in forskolin/Mn^{2+}-stimulated AC in S49 cyc-membranes). A more lipophilic, fluorescent derivative of the GTP-hydrolysis-resistant GTP analog, GTPγS (Cat. No. 371545). Useful for investigating the interactions of low molecular weight GTP-binding proteins with their specific effector proteins. Supplied as a 5 mM solution in H2O. *Purity: ≥90% by HPLC.* M.W. 976.0

Cat. No. 444169 **50 µl** **€ 266**

Ref.: Gille, A., and Seifert, R. 2003. *J. Biol. Chem.* **278**, 12672; Remmers, A.E., et al. 1999. *Biochemistry* **38**, 13795; Lan, K.L., et al. 1998. *Biochemistry* **37**, 837; Remmers, A.E. 1998. *Anal. Biochem.* **257**, 89.

NEW! Tools for Neurodegenerative Disease Research

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

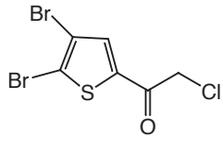
GSK-3β is a dual specificity kinase that plays important roles in insulin- and Wnt-mediated cellular signalings. Plays a major role in destabilizing microtubules by its ability to phosphorylate the tau protein. Contains both an N- and a C-terminal His•Tag® sequence. *Biological activity: 1 mg GSK-3β maximally phosphorylates 100 ng Tau protein in 30 minutes at 30°C, pH 7.5. Purity: ≥90% by SDS-PAGE.*

Cat. No. 361524 **100 µg** **€ 392**

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

GSK-3β Inhibitor VI [2-Chloro-1-(4,5-dibromo-thiophen-2-yl)-ethanone]

A cell-permeable, irreversible, and non-ATP competitive inhibitor of GSK-3β (IC_{50} = 1 µM). This reactive alkylating agent is selective towards GSK-3β and does not affect PKA activity even at concentrations as high as 100 µM. *Purity: ≥95% by HPLC.* M.W. 318.4.

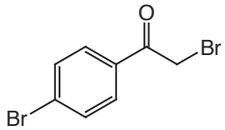


Cat. No. 361547 **5 mg** **€ 110**

Ref.: Conde, S., et al. 2003. *J. Med. Chem.* **46**, 4631.

GSK-3β Inhibitor VII (α-4-Dibromoacetophenone)

A phenyl α-bromomethyl ketone compound that acts as a cell-permeable, irreversible, and non-ATP competitive inhibitor of GSK-3β (IC_{50} = 500 nM). This reactive alkylating agent is selective towards GSK-3β and does not affect PKA activity even at concentrations as high as 100 µM. *Purity: ≥98% by HPLC.* M.W. 277.9.

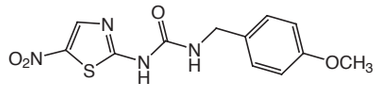


Cat. No. 361548 **5 mg** **€ 100**

Ref.: Conde, S., et al. 2003. *J. Med. Chem.* **46**, 4631.

GSK-3β Inhibitor VIII [N-(4-Methoxybenzyl)-N′-(5-nitro-1,3-thiazol-2-yl)urea]

A cell-permeable, potent, ATP-competitive, and highly specific inhibitor of GSK-3β (IC_{50} = 104 nM; K_i = 38 nM). Its specificity has been confirmed using a panel of 28 kinases, including Cdk2 and Cdk5 (IC_{50} > 100 µM). *Purity: ≥95% by HPLC.* M.W. 308.3.

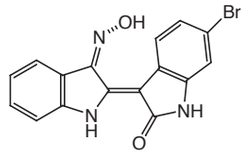


Cat. No. 361549 **5 mg** **€ 100**

Ref.: Bhat, R., et al. 2003. *J. Biol. Chem.* **278**, 45937.

GSK-3 Inhibitor IX (BIO)

A cell-permeable, highly potent, selective, reversible, and ATP-competitive inhibitor of GSK-3α/β (IC_{50} = 5 nM). Its specificity has been tested against various Cdks (IC_{50} = 83, 300, 320, and 10,000 nM for Cdk5/p25, Cdk2/cyclin A, Cdk1/cyclin B, and Cdk4/cyclin D1, respectively) as well as many other commonly studied kinases. *Purity: ≥97% by HPLC.* M.W. 356.2.



Cat. No. 361550 **1 mg** **€ 112**

Ref.: Polychronopoulos, P., et al. 2004. *J. Med. Chem.* **47**, 935. Sato, N., et al. 2004. *Nat. Med.* **10**, 55. Meijer, L., et al. 2003. *Chem. Biol.* **10**, 1255.

γ-Secretase Inhibitor XIX

A cell-permeable, highly potent γ-secretase inhibitor (IC_{50} = 60 pM towards $Aβ_{40}$ secretion in SH-SY5Y cells overexpressing spβA4CTF). Supplied as a 5 mM solution (100 µg/37 µl) in DMSO. *Purity: ≥95% by HPLC.* M.W. 543.5.

Cat. No. 565787 **100 µg** **€ 206**

Ref.: Churcher, I., et al. 2003. *J. Med. Chem.* **46**, 2275.

NEW! γ-Secretase Substrate, Fluorogenic [NMA-GGVVIATVK(DNP)-*D*R*D*R*D*R-NH_2]
An internally quenched fluorogenic peptide substrate containing the C-terminal amino acid sequence (derived from amyloid β-peptide precursor protein) that is cleaved by γ-secretase. Shown to be sensitive and useful for assaying γ-secretase activity. The proteolysis at the $Aβ_{40}$-, $Aβ_{42}$-, and $Aβ_{43}$-generating cleavage sites results in enhanced fluorescence. *Purity: ≥95% by HPLC.* M.W. 1609.9.

Cat. No. 565764 **1 mg** **€ 114**

Ref.: Farmery, M.R., et al. 2003. *J. Biol. Chem.* **278**, 24277.

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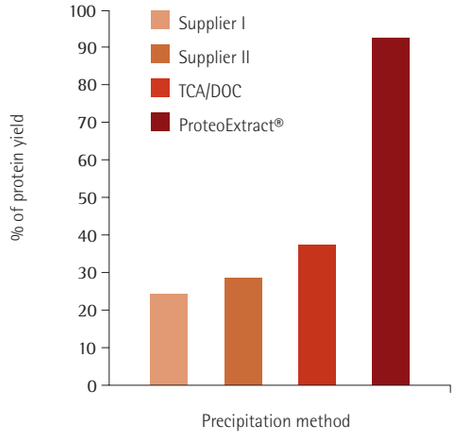
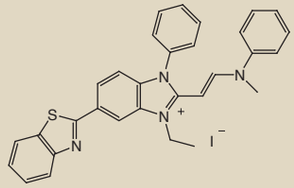
ProteoExtract® Protein Precipitation Kit
This kit is designed for fast and efficient concentration and clean-up of protein samples from aqueous samples. Protein solutions obtained exhibit very low conductivity. Detergents, chaotropes, buffer reagents, salts and other interfering compounds remain in solution. Precipitated proteins can be resuspended in a buffer and used for a wide range of applications, including isoelectric focusing, 2D-gel electrophoresis, and tryptic digestion prior to mass spectrometry and peptide separation.

Cat. No. 539180 **1 kit** **€ 209**



Protein yields obtained after processing samples with common precipitation methods. Protein at a concentration of 2 mg/ml was precipitated using the ProteoExtract® Kit. Protein pellets were redissolved in IEF buffer prior to determination of protein concentration. The same experiment was performed in parallel using TCA/DOC and products from Supplier I and Supplier II. All experiments were performed in duplicate. The ProteoExtract® Protein Precipitation Kit delivered up to 3 times greater protein yields as compared to other precipitation methods.

Akt Inhibitor IV
A cell-permeable inhibitor of Akt phosphorylation/activation that acts by targeting the ATP binding site of a kinase upstream of Akt, but downstream of PI3K. *Purity: ≥98% by HPLC.* M.W. 614.6.



Cat. No. 124011 **1 mg** **€ 110**
5 mg **€ 398**

Ref.: Kau, T.R., et al. 2003. *Cancer Cell* **4**, 463.

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ProteoExtract® All-in-One Trypsin Digestion Kit

Designed for tryptic digestion of proteins that are isolated from SDS-PAGE gels or from extracts. Kit includes an affinity-purified sequencing grade trypsin devoid of any residual chymotrypsin or other protease activities. Can be used with polyacrylamide gels stained with Coomassie™ Brilliant blue, SYPRO® Ruby, or Pro-Q® Diamond dyes for phosphoprotein/peptide detection.

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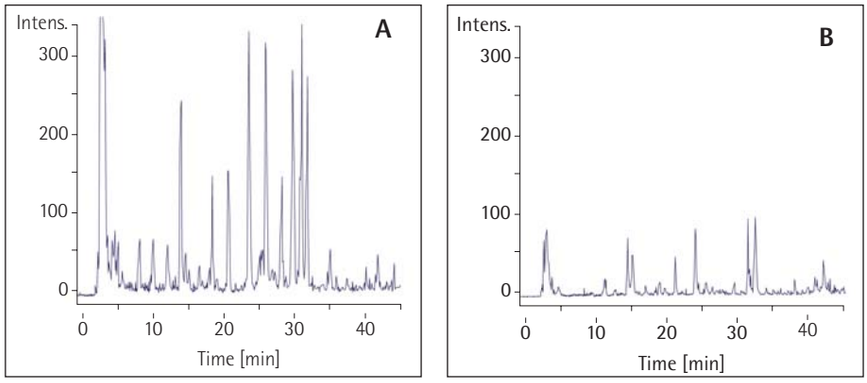
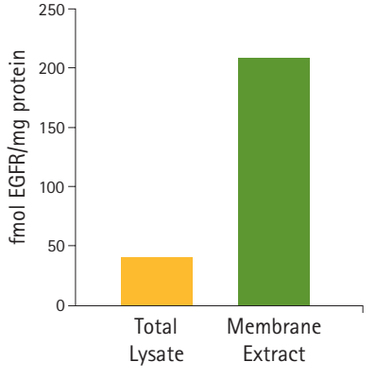


Ovalbumin was digested using ProteoExtract® All-in-One Trypsin Digestion Kit (A) or according to Supplier Z kit protocol (B). Base peak chromatograms of nanoLC/MS runs are shown.

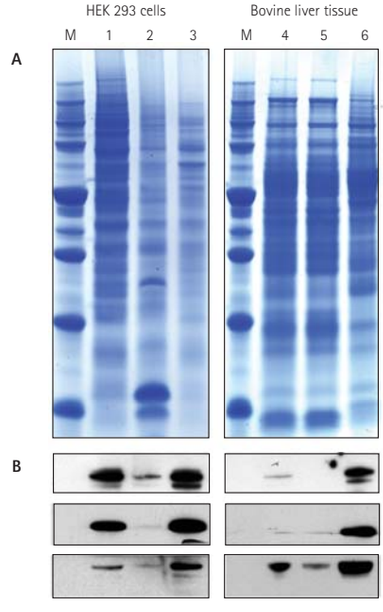
ProteoExtract® Native Membrane Protein Extraction Kit (M-PEK)

Designed for the isolation of native membrane proteins from mammalian cells and tissue. This kit provides 3-5 fold enrichment of integral membrane and membrane-associated proteins under non-denaturing conditions. M-PEK is easy to use and allows for a fast and robust two-step extraction of membrane proteins. M-PEK extracted membrane proteins generally do not require dialysis and in most cases can be used directly for downstream applications. Optimized protocols are provided for adherent tissue culture cells, suspension grown tissue culture cells, frozen cell pellets, and tissue.

Cat. No. 444810 **1 kit** **€ 280**



HEK 293 cells were extracted with buffered 1% Triton® X-100 to generate a total lysate or extracted with M-PEK to yield a membrane fraction. Equal sample volumes of total lysate and membrane fraction were normalized by total protein concentration in the sample, and used to quantify the EGF receptor (EGFR) concentrations. The membrane extract obtained with the M-PEK demonstrated a 4.5-fold enrichment of EGFR.



Selective extraction of membrane proteins from cells and tissue samples

A. HEK 293 suspension cells and frozen bovine liver tissue were extracted either with SDS to yield a total lysate or with M-PEK to yield a membrane fraction and remaining "nonmembranous" proteins. Protein equivalents of extracted fractions were separated by SDS-PAGE and visualized by Coomassie blue staining. The membrane protein pattern (lanes 3 and 6) is clearly distinct from the patterns of both total and nonmembranous fractions (lanes 1, 2, 4, and 5), indicating the selectivity of the M-PEK extraction.

B. Immunoblotting of an equivalent gel using membrane-associated and integral membrane protein markers demonstrates the selectivity of the M-PEK extraction procedure.

ProteoExtract® Detergent Set

A set containing nonionic and zwitterionic detergents for membrane protein solubilization for two-dimensional electrophoresis. The set includes 10 g of TRITON® X-100 Detergent (Cat. No. 648462) and 1 g each of ASB-14 (Cat. No. 182750), ASB-14-4 (Cat. No. 182751), ASB-16 (Cat. No. 182755), ASB-C8Ø (Cat. No. 182730), CHAPS (Cat. No.

Cat. No. 539751 **1 Set** **€ 479**

D-Tube™ Dialyzers

D-Tube™ Dialyzers

The D-Tube™ Dialyzers can be used for dialysis and electroelution of proteins, RNA, DNA and oligonucleotides from polyacrylamide or agarose gels. The disposable, single-use tubes require no syringes, microcentrifuge, or laborious steps to manipulate small sample volumes. The sample is added and removed using a standard laboratory pipette. Available with the molecular weight cut-offs from 3.5 to 14 kDa, the D-Tube Dialyzers are designed in three volume capacities: mini (10-250 µl), midi (50-800 µl) and maxi (100-3000 µl). The membrane is ultra-clean, EDTA-treated regenerated cellulose, sulfur- and heavy metal-free. Each kit contains 10 D-Tubes and one floating rack that can hold up to four D-Tubes in the exchange buffer.

Features:

- Easy-to-handle dialyzers for buffer exchange, removal of urea, detergents, ethidium bromide
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- Proteases, RNAse, DNAse and PCR product free.
- Ideal for electro-elution of proteins, protein-DNA complexes, oligonucleotides, DNA and RNA from polyacrylamide and agarose gels

D-Tube™ Electroelution Accessory Kit, Midi

The combination of D-Tube Dialyzers and D-Tube Electroelution Accessory Kit provides a unique tool for extraction of any protein, protein-protein and protein-DNA complexes from non-denaturing and denaturing (SDS) polyacrylamide gels, and for oligonucleotides, RNA and DNA extraction from both polyacrylamide and agarose gels. The D-Tube™ Electroelution Accessory Kit provides one D-tube supporting tray that fits into most commercially-available horizontal electrophoresis units and optimized reagents for protein and nucleic acid precipitation following electroelution.

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- More than 60% protein recovery in less than 2 hours
- More than 90% recovery of oligonucleotides, RNA and DNA from 15 nucleotides to 80 kbp
- Procedure compatible with variety of downstream applications including MALDI-MS, functional assays, HPLC
- High-throughput electroelution from multiple samples simultaneously

Product	Cat. No.	Size	Price €
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D-Tube™ Dialyzer Mini, MWCO 12-14 kDa	**71505-3**	1 kit (10 tubes)	54
D-Tube™ Dialyzer Midi, MWCO 3.5 kDa	**71506-3**	1 kit (10 tubes)	83
D-Tube™ Dialyzer Midi, MWCO 6-8 kDa	**71507-3**	1 kit (10 tubes)	83
D-Tube™ Dialyzer Maxi, MWCO 3.5 kDa	**71508-3**	1 kit (10 tubes)	99
D-Tube™ Dialyzer Maxi, MWCO 6-8 kDa	**71509-3**	1 kit (10 tubes)	102
D-Tube™ Dialyzer Maxi, MWCO 12-14 kDa	**71510-3**	1 kit (10 tubes)	99
D-Tube™ Electroelution Accessory Kit Midi	**71511-3**	1 kit	52

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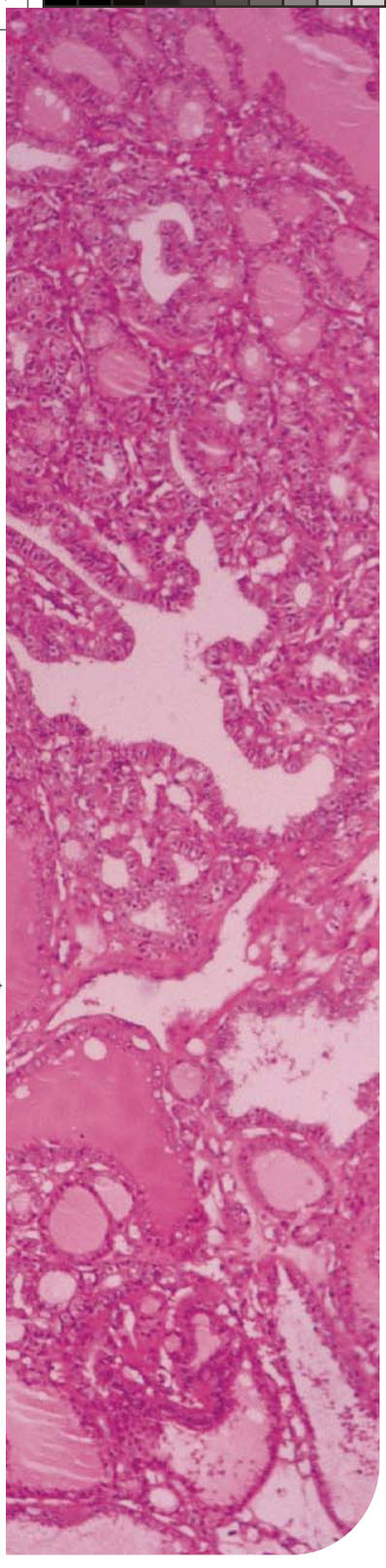

Stem Cells: The Future of Repair, Replacement, and Regeneration

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

A major emphasis in stem cell research is placed on controlled differentiation of stem cells into a desired cell or tissue type. It is well recognized that several growth and differentiation factors are responsible for shaping the destiny of stem cells. For example, TGF-β family members are shown to have significant effect on the differentiation of ESCs and neural crest stem cells. Wnt signaling also plays an important supportive role in cell differentiation. Integral membrane proteins and integrins also contribute to the microenvironment of stem cells in shaping their destiny. Researchers have used FGF-2 and Sonic Hedgehog (Shh) to obtain dopaminergic and serotonergic neurons from mouse ESCs.

Although the pluripotent ESCs have an important advantage over adult stem cells, ethical debates have limited research on ESCs. Some advances have been made in the isolation and characterization of adult stem cells. In adults, hematopoietic stem cells (HSCs) proliferate and differentiate throughout the life cycle to produce lymphoid and myeloid cell types. Interleukin-3 and 6, thrombopoietin, stem cell factor (SCF), and Flt-3 Ligand have been used as potential candidates for unspecific hematopoietic stimulation. In addition, bone marrow-derived stem cells are shown to differentiate into various cell types, including adipocytes, chondrocytes, osteocytes, hepatocytes, and cardiomyocytes. In the nervous system, the plastic property of neural stem cells has been exploited to regenerate neural tissues lost to injury or neurodegenerative diseases.

References:

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McKay, R. 2000. *Nature* **406**, 361.

NEW! Tools for Cellular Differentiation and Stem Cell Research

Product	Cat. No.	Comments	Size	Price €
Cardiogenol C	**217460**	A cell-permeable pyrimidine compound that potently induces the differentiation of embryonic stem cells into cardiomyocytes (EC_{50} = 100 nM).	5 mg	168
Cyclopamine, *V. californicum*	**239803**	A natural alkaloid that acts as a specific Sonic Hedgehog signaling (Shh) antagonist. Acts at the level of Smoothened (Smo).	1 mg	144
Cyclopamine-KAAD	**239804**	A potent analog of Cyclopamine (Cat. No. 239803) that specifically inhibits the Hedgehog (Hh) signaling with similar or lower toxicity (IC_{50} = 20 nM in Shh-LIGHT2 assay; 50 nM in p2Ptch$^{-/-}$ cells; 500 nM in SmoA1-LIGHT cells). Binds to SmoA1 and promotes its exit from the endoplasmic reticulum. Suppresses both the ShhNp-induced pathway activity and SmoA1-induced reporter activity.	100 µg	153
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	110
Purmorphamine	**540220**	A cell-permeable purine compound that induces osteoblast differentiation of multipotent mesenchymal progenitor cells C3H10T1/2 (EC_{50} = 1 µM) and lineage-committed preosteoblasts MC3T3-E1. Its effect can be synergized with that of bone morphogenetic protein-4.	5 mg	168
Reversine	**554717**	A cell-permeable purine analog that acts as a dedifferentiation-inducing agent. Shown to induce mouse C2C12 myoblast cells to become multipotent mesenchymal progenitor cells in the concentration range of 1 - 10 µM.	5 mg	168
SANT-1	**559303**	A potent antagonist of the Sonic Hedgehog signaling pathway (IC_{50} = 20 nM in the Shh-LIGHT2 assay and in Ptch1$^{-/-}$ cells] by binding directly to Smoothened (Smo; K_d = 1.2 nM).	5 mg	133
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	154
Stem Cell Factor, Human, Recombinant, *E. coli*	**569600**	A hematopoietic growth factor that stimulates the growth of cells of multiple lineage. Biological activity: ED_{50} = 2.5 - 5.0 ng/ml as measured in a cell proliferation assay using a factor-dependent human erythroleukemic cell line.	10 µg	365
Stem Cell Factor, Mouse, Recombinant, *E. coli*	**569610**	A hematopoietic growth factor. Biological activity: ED_{50} = 5.0 - 10.0 ng/ml as measured in a cell proliferation assay using a factor-dependent human erythroleukemic cell line.	10 µg	365

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Microcystin-LR, *Microcystis aeruginosa* NEW! Low Price

A potent inhibitor of protein phosphatase 1 (PP1) and protein phosphatase 2A (PP2A). Unlike Okadaic Acid (Cat. No. 495604), Microcystin-LR is effective on both PP1 (IC_{50} = 1.7 nM) and PP2A (IC_{50} = 40 pM). Reacts with phosphatase in a two-step mechanism involving rapid binding and inactivation of the catalytic subunit followed by slower covalent interactions. *Purity: ≥95% by HPLC. Not available for sale outside of the United States without an export license from the U.S. Department of Commerce.*

Cat. No. 475815 **500 µg** **€ 252**

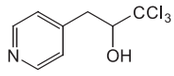
Xestospongin C, *Xestospongia sp.*

A cell-permeable, potent, and reversible blocker of IP_3-mediated Ca^{2+} release (IC_{50} = 358 nM). Does not interact with the IP_3-binding site. Displays high selectivity over the skeletal isoform of the ryanodine receptor type 1 (RyR-1). *Purity: ≥90% by TLC.*

Cat. No. 682160 **10 µg** **€ 188**

NEW! Tools for Apoptosis Research

Apoptosis Activator I [α-(Trichloromethyl)-4-pyridineethanol]

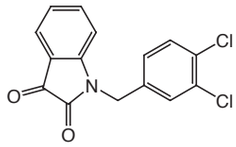


A cell-permeable pyridyl compound that selectively promotes apoptosome formation and subsequent caspase activation by antagonizing prothymosin-α (ProT), a negative regulator of mitochondria-initiated caspase activation. *Purity: ≥98% by HPLC.* M.W. 240.5.

Cat. No. 178491 **5 mg** **€ 81**

Ref.: Nguyen, J.T., and Wells, J.A. 2003. *Proc. Natl. Acad. Sci. USA* **100**, 7533; Jiang, X., et al. 2003. *Science* **299**, 223; Nicholson, D.W., and Thornberry, N.A. 2003. *Science* **299**, 214.

Apoptosis Activator II



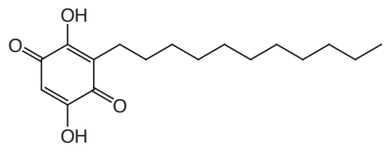
A cell-permeable indoledione compound that activates caspases in a cytochrome *c*-dependent manner and induces apoptosis in tumor cells by promoting the oligomerization of Apaf-1 into the mature apoptosome. *Purity: ≥95% by HPLC.* M.W. 306.1.

Cat. No. 178492 **5 mg** **€ 100**

Ref.: Nguyen, J.T., and Wells, J.A. 2003. *Proc. Natl. Acad. Sci. USA* **100**, 7533

Apoptosis Activator III, Embelin (XIAP inhibitor)

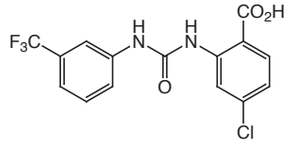
A nonpeptidic, cell-permeable compound that specifically antagonizes XIAP-mediated inhibition of caspase-9 activation by directly targeting the Smac and caspase-9 binding domain BIR3 (IC_{50} = 4.1 µM in a competitive binding assay with Smac peptide). Shown to induce caspase-9-mediated apoptosis in prostate cancer cells with high levels of XIAP (IC_{50} = 3.7 and 5.7 µM for PC-3 and LnCap, respectively), while exhibiting much less effect towards cells with low levels of XIAP (IC_{50} = 19.3 and 20.1 µM for WI-38 and PrEC, respectively). M.W. 294.4.



Cat. No. 178493 **10 mg** **€ 104**

Ref.: Nikolovska-Coleska, Z., et al. 2004. *J. Med. Chem.* **47**, 2430

Apoptosis Inhibitor II, NS3694



A cell-permeable diarylurea compound that specifically prevents the active ~700 kDa apoptosome complex formation triggered by cytochrome *c* release. Protects against apoptosome-mediated caspase activation and cell death (50 µM completely blocks TNF-α-induced death in MCF-casp3 cells). Does not affect apoptosome-independent caspase activation and cell death induced by FasL. Has no effect on cytochrome *c* release and activity of caspases. *Purity: ≥98% by HPLC.* M.W. 358.7.

Cat. No. 178494 **10 mg** **€ 116**

Ref.: Lademann, U., et al. 2003. *Mol. Cell. Biol.* **23**, 7829.

Fas/FasL Antagonist, Kp7-6 (H-YC*DEHFC*Y-OH, Cyclic [Cys-Cys disulfide])

An exocyclic cystine-knot peptide that specifically antagonizes Fas/FasL-mediated cellular apoptotic signals (58% reduction of FasL-induced apoptosis in Jurkat cells at 1 mg/ml). Binds to FasL (Cat. Nos. PF033 and PF092) and Fas (CD95/APO 1) with comparable affinity (K_d = 11.2 and 13.2 µM, respectively), resulting in disabled receptor ensembles and altered signaling pathways. *Purity: ≥98% by HPLC.* M.W. 1077.2.

Cat. No. 341291 **25 mg** **€ 281**

Ref.: Hasegawa, A., et al. 2004. *Proc. Natl. Acad. Sci. USA* **101**, 6599.

Bax Channel Blocker [(±)-1-(3,6-Dibromocarbazol-9-yl)-3-piperazin-1-yl-propan-2-ol, bis TFA]

A cell-permeable dibromocarbazolo-piperazinyl derivative that effectively blocks Bid-induced cytochrome *c* release from HeLa cell mitochondria (~80% inhibition at 5 µM) by inhibiting Bax channel-forming activity (IC_{50} = 520 nM in a liposome channel assay). *Purity: ≥98% by HPLC.* M.W. 695.3.

Cat. No. 196805 **5 mg** **€ 100**

Ref.: Bombrun, A., et al. 2003. *J. Med. Chem.* **46**, 4365.

Caspase-3/7 Inhibitor II (Ac-DNLD-CHO)

A tetrapeptidyl aldehyde that acts as a potent, reversible and active site binding inhibitor of caspases-3 and -7 (IC_{50} = 3.2 nM and 22.6 nM, respectively) and displays ~ 100-fold greater selectivity over caspases-8 and -9 (IC_{50} = 577.6 nM and 364.7 nM, respectively). Offers protection against Camptothecin (Cat. No. 208925), and anti-Fas-mediated apoptosis in Jurkat T cells. M.W. 501.5.

Cat. No. 218832 **1 mg** **€ 104**

Ref.: Yoshimori, A., et al. 2004. *BMC Pharmacol.* **4**, 7.

p53 Activator II, Cell-Permeable (RI-TATp53C-WT, D-isomer)

A cell-permeable and proteolytically stable p53-activating peptide that displays antitumor properties. Activates p53-dependent gene transcription and inhibits tumor cell proliferation in a p53-dependent manner, while exhibiting no effect on the proliferation of normal cells expressing wild-type p53. *Purity: ≥95% by HPLC.* M.W. 4031.6.

Cat. No. 506144 **500 µg** **€ 306**

Ref.: Snyder, E.L., et al. 2004. *PLoS Biol.* **2**, 186.

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InnoZyme™ Granzyme B Immunocapture Activity Assay Kit

A sensitive and specific fluorogenic assay kit for Granzyme B based on the QuickZyme™ technology platform where modified pro-urokinase serves as a substrate for Granzyme B. Cleavage by Granzyme B activates the urokinase which in turn cleaves the fluorogenic urokinase substrate (Glutaryl Gly-Arg-AMC; Ex. max.: 360-380 nm; Em. max.: 460-480 nm). Specificity is increased through the immunocapture of Granzyme B on the 96-well plate.

Cat. No. CBA014 **1 kit** **€ 640**

Apoptosis Myosin Cleavage Detection Kit

A convenient assay for the detection of apoptosis in human cell samples. During apoptosis, nonmuscle myosin (NMM) heavy chain is cleaved by caspases from 226 kDa to 150 kDa. Treated cells are lysed in the buffer provided and proteins are separated via SDS-PAGE, and heavy chain cleavage is detected via immunoblot.

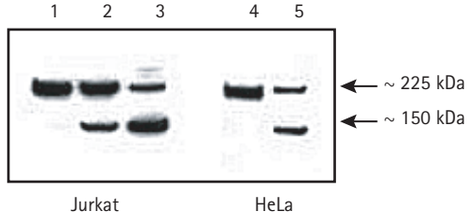

Figure 1: Detection of cleaved NMM in cell lysates of apoptotic Jurkat or HeLa cells by Western blot. Apoptosis was included by treatment with camptothecin.
Lane 1: Untreated Jurkat cells.
Lane 2: Jurkat cells treated with 5 µg/ml camptothecin for 5 h.
Lane 3: Jurkat cells treated with 5 µg/ml camptothecin for 16 h.
Lane 4: Untreated HeLa cells.
Lane 5: HeLa cells treated with 5 µg/ml camptothecin for 16 h.

Cat. No. CBA015 **1 kit** **€ 275**

NEW! Antibodies for Apoptosis Research

Product	Cat. No.	Comments	Size	Price €
Anti-p53, Phospho-Specific (Ser^{20}), Human (Rabbit)	**DR1023**	Immunoaffinity-purified. Immunogen used was a synthetic phosphopeptide corresponding to amino acid residues surrounding Ser^{20} of p53. Detects ~p53 when phosphorylated on Ser^{20}. Phosphorylation of Ser^{20} and Ser^{15} occurs as a result of DNA damage leading to reduced interaction of p53 with its negative regulator, MDM2. **IB**, **IC**, **PS**	50 µl	202
Anti-p53, Phospho-Specific (Ser^{46}), Human (Rabbit)	**DR1024**	Immunoaffinity-purified. Immunogen used was a synthetic phosphopeptide corresponding to amino acid residues surrounding Ser^{46} of p53. Detects p53 when phosphorylated on Ser^{46}. Phosphorylation of Ser^{46} is believed to be important in regulating the ability of p53 to induce apoptosis. **IB**, **IC**, **IP**	50 µl	202
Anti-PARC/H7-AP1, Human (Rabbit)	**DR1028**	Immunoaffinity-purified. Immunogen used was a synthetic peptide corresponding to amino acid residues between 900 and 950 of PARC (locus link #23113). Detects the ~270 kDa PARC/H7-AP1, a Parkin-like ubiquitin ligase that serves as a cytoplasmic anchor for p53. Supplied at 1 mg/ml. **IB**, **IP**	100 µg	337

IB: immunoblotting; **IC**: immunocytochemistry; **IP**: immunoprecipitation: **PS**: paraffin sections

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Aberrant glycosylation of membrane components is a common feature of carcinoma cells and is reportedly associated with invasion and metastasis. An elevation α2,6-sialyltransferase activity and an increased α2,6-sialylation of cell membranes are among the most prominent glycosylation changes associated with tumor growth and metastasis. Also, α-2,3-linked sialic acid residues are shown to increase significantly from stage I to stage II tumors.

α2,3-(N)-Sialyltransferase, Rat, Recombinant, *Spodoptera frugiperda*

A soluble recombinant form of rat liver α2,3-NST from specific for Galβ1,3- and Galβ1,4GlcNAc. *Specific activity: ≥1 unit/mg protein.* M.W. 39,000.

Cat. No. 566218 **100 mU** **€ 113**
500 mU **€ 429**

Ref.: Williams, M.A., et al. 1995. *Glycoconj. J.* **12**, 755. Sold under license of U.S. Patent 5,032,519.

α2,6-(N)-Sialyltransferase, Rat, Recombinant, *Spodoptera frugiperda*

A soluble recombinant form of rat liver α2,6-NST from rat liver. *Specific activity: ≥1 unit/mg protein.* M.W. 41,000.

Cat. No. 566222 **100 mU** **€ 235**

Ref.: Williams, M.A., et al. 1995. *Glycoconj. J.* **12**, 755; Colley, K.J., et al. 1989. *J. Biol. Chem.* **264**, 17619. Sold under license of U.S. Patent 5,032,519.

α2,3-(O)-Sialyltransferase, Rat, Recombinant, *Spodoptera frugiperda*

A soluble recombinant form of rat liver α2,3-OST. *Specific activity: ≥1 unit/mg protein.* M.W. 40,000.

Cat. No. 566227 **100 mU** **€ 98**

Ref.: Lee, Y.-C., et al. 1994. *J. Biol. Chem.* **269**, 10028. Sold under license of U.S. Patent 5,032,519.

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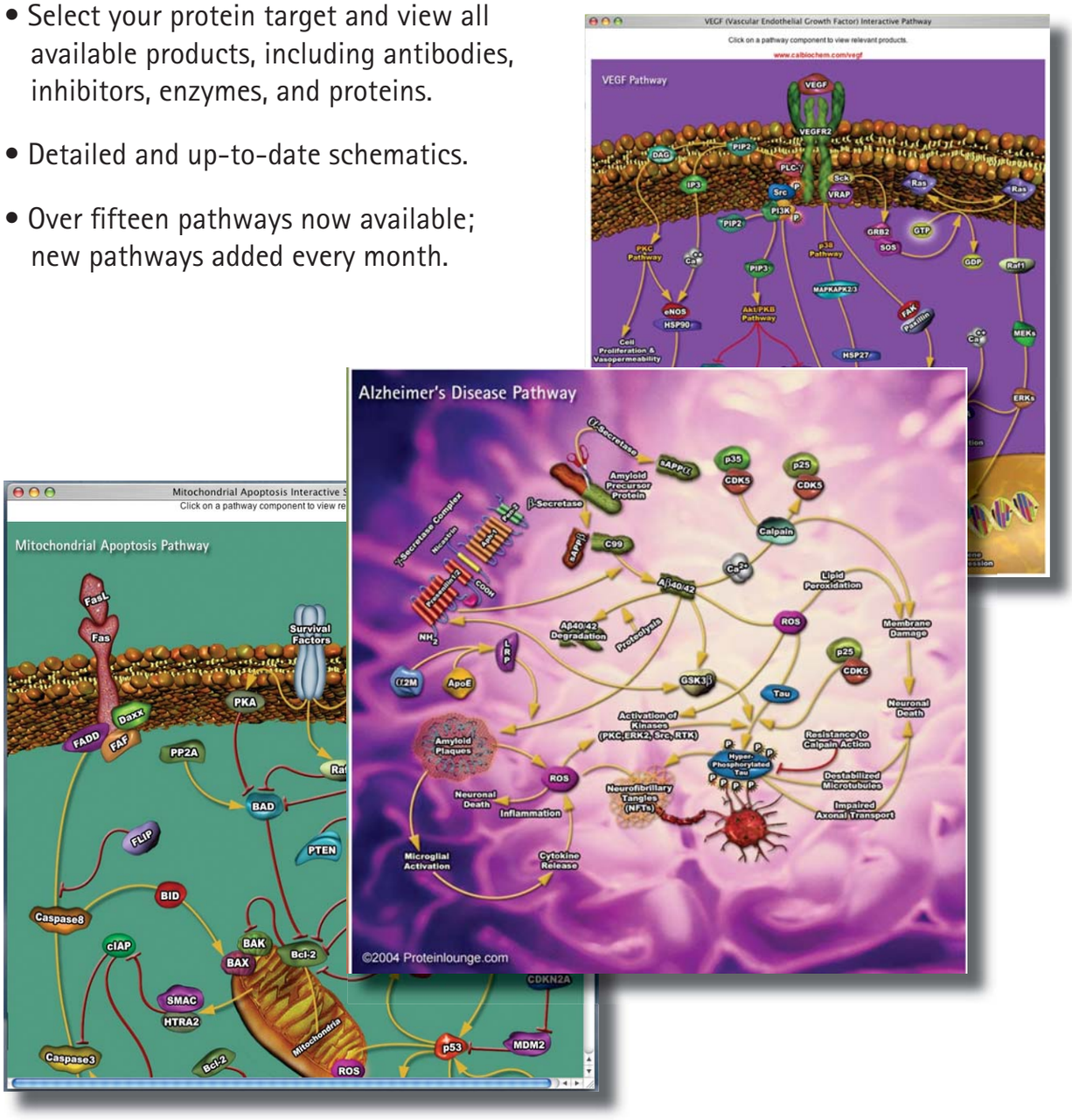

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