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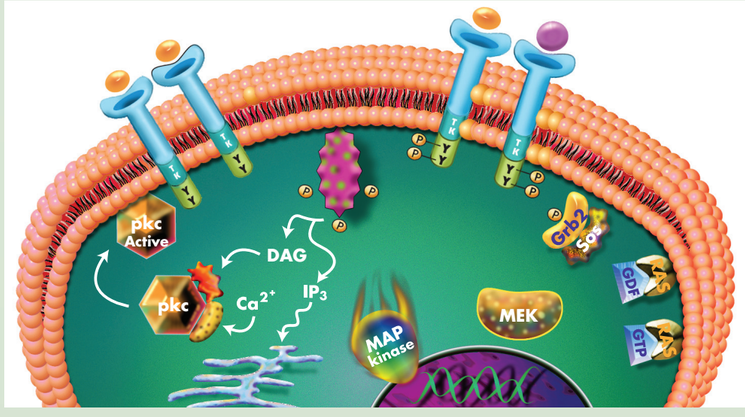
Volume 28, Number 2, 2002

Protein Tyrosine Kinases : Rational Targets for Cancer Therapy

Protein tyrosine kinases (PTK), a group of tightly regulated enzymes, play a key role in the regulation of cell proliferation, differentiation, metabolism, migration, and survival. They are also frequent targets of oncogenic mutations leading to dysregulated tyrosine kinase activity and subsequently tumor progression. Unregulated activation or overexpression of PTKs has been linked to various forms of cancers and benign proliferative conditions. PTKs have been classified into receptor PTKs and non-receptor PTKs. Receptor PTKs contain a single polypeptide chain with a transmembrane segment. The extracellular end of this segment contains a high affinity ligand-binding domain, while the cytoplasmic end comprises the catalytic core and the regulatory sequences. The cytosolic end also contains tyrosine residues, which become substrates or targets for the tyrosine kinase portion of the receptor. The transmembrane domain anchors the receptor in the plasma membrane, while the extracellular domain binds the growth factor.

The PTK remains inactive until a ligand binds to the receptor, which leads to the dimerization of two ligand-bound receptors. The only exception to the dimerization scheme is the activation of insulin receptor, which exists in a natural dimerized state (α, β subunits). Once activated, receptors are able to autophosphorylate tyrosine residues outside the catalytic domain. This autophosphorylation stabilizes the active receptor conformation and creates phosphotyrosine-docking sites for proteins that transduce signals within the cell. The unphosphorylated receptor lacks the accurate conformation for recognition. The cytosolic portion of phosphorylated receptor is capable of recruiting a number of cytosolic adapter proteins via interactions between phosphorylated tyrosine residues on the receptor and the SH2 (Src homology 2) domain on the adapter molecule. The SH2 domains contain a stretch of amino acids, which can recognize phosphotyrosines on the receptor. Several signaling proteins, such as Ras-GAP, PI3-kinase, and phospholipase C, can bind to the intracellular domain of receptor PTKs in a phosphotyrosine-dependent manner. It is worth noting here that different proteins have different SH2 domains that recognize specific phosphotyrosine residues. An SH2-containing protein, Grb2, acts as a common adapter protein in a majority of growth factor related signaling events.

Grb2 binding to phosphotyrosine residues changes its conformation and allows it to bind to proline-rich sequences in the carboxy terminal tail of Sos,



Contents

a GDP-GTP exchange protein. This binding displaces an inhibitory domain in Sos and allows the activation of Sos, which then translocates to the plasma membrane to cause an exchange of GDP for GTP and activates Ras. A wide variety of effectors of Ras activation have been reported, however, activation of Raf, a cytoplasmic protein kinase, is one of the best studied examples. Ras binds to the N-terminus of Raf and recruits it to the inner surface of the plasma membrane, where it is phosphorylated by protein kinase C. Translocation of Raf to the membrane positions it in direct proximity of MAP kinase kinase (MEK). Raf phosphorylates MEK, which in turn phosphorylates MAP kinase (MAPK). In a resting cell MAPK remains inactive because its phosphorylation lip excludes ATP access to the binding pocket. However, MEK binding destabilizes the lip and exposes the buried tyrosine residues. Phosphorylation of the exposed tyrosine and nearby threonine residue causes the lip to alter its conformation allowing ATP binding.

Our discussion so far has been limited to receptors with intrinsic tyrosine kinase activities. However, in some cases the receptor and the tyrosine kinase are two separate proteins. Such tyrosine kinases are referred to as the non-receptor or cellular PTKs. They include members of the Src, Tec, JAK, Fes, Abl, FAK, Csk, and Syk families. They are located in the cytoplasm as well as in the nucleus and play important roles in cellular signaling. They are also activated by a large number of stimuli, including hormones, neurotransmitters, growth factors, and cytokines. While there is a striking homology in the catalytic sequences of these enzymes, they diverge greatly in their regulatory and non-enzymatic sequences. They exhibit distinct kinase regulation, substrate phosphorylation, and function. For example, Src is involved in cell differentiation, whereas Abl is involved in growth inhibition, and FAK activity is linked with cell adhesion. Deregulation of these kinases has also been linked to several human diseases. For example, oncogenic forms of Abl, JAK, and Src kinases have been reported in several human cancers and are shown to be involved in carcinoma development.

Unlike the receptor PTK, not much is known about the mechanism of activation of non-receptor PTKs. In most cases, their activation also begins with the phosphorylation of a tyrosine residue present in an activation loop. The best studied enzymes in this group include Src kinases. Src is believed to be negatively regulated by phosphorylation at Tyr^{527} present at the C-terminus by Csk and other cellular kinases. The enzyme assumes an inactive conformation when this phosphotyrosine is bound by the Src SH2 domain in an intramolecular fashion. In this structure, the Src SH3 domain interacts with a single proline, Pro^{250}, in the linker region between the SH2 and catalytic domain. In contrast to Src activation, c-Abl kinase activity is stimulated by phosphorylation of a catalytic domain tyrosine residue, Tyr^{412}, either via autophosphorylation or via transphosphorylation by c-Src. Recent studies have indicated that dimerization or oligomerization of c-Abl might also be sufficient to activate Abl kinase activity *in vivo*. Syk, an essential enzyme for immune system development and function, is reportedly activated by binding to diphosphorylated immune receptor tyrosine-based activation motifs (pITAMs). More recently, it is also shown to be activated by binding to the cytoplasmic tail of the integrin β3 receptor through its SH2 domain.

Due to their involvement in various forms of cancers, PTKs have become prominent targets for therapeutic intervention. Selective receptor and non-receptor PTK inhibitors represent a promising class of anti-tumor agents. Using the structure-based designs, several new therapeutic agents have been developed that mimic the EGFR kinase domain. These agents are shown to inhibit multiple features of cancer cells, including proliferation, survival, invasion, and angiogenesis. For example, quinazoline compounds, such as PD 168393 (**Cat. No. 513033**) and PD156273 (**Cat. No. 513032**) are highly potent and selective inhibitors of EGF receptor tyrosine kinase activity and are shown to block tumor cell growth both *in vitro* and *in vivo*. Selected indolinone compounds, such as SU6656 (**Cat. No. 572635**), have been shown to be potent and selective inhibitors of Src family of non-receptor tyrosine kinases. It is important to note that signals from various pathways may converge to bring about a desired effect in the cell in a synergistic manner. For example, the stimulation of cell proliferation may occur by a combination of receptor PTK activation, activation of non-receptor PTKs and G-protein-coupled receptors. Sub-threshold combinations of various ligands can act synergistically to stimulate the action of downstream effectors to fully promote a biological response.

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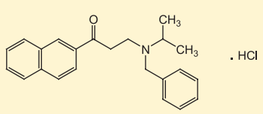
New! JAK3 Inhibitors

JAK3 Inhibitor 4

(2-Naphthyl-(N-isopropyl,N-benzyl)-β-aminoethylketone, HCl; ZM 39923)

A β-(aminoethyl)ketone based prodrug that acts as a potent and selective ATP-competitive inhibitor of JAK3 (pIC_{50} of 7.1). A weak inhibitor of other tyrosine kinases (pIC_{50} = 5.6 for EGFRK and 4.4 for JAK1). M.W. 367.9.



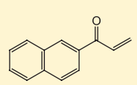
Cat. No. 420121 **10 mg** **$ 175**

Ref.: Brown, G.R., et al. 2000. *Bioorg. Med. Chem. Lett.* **10,** 575.

JAK3 Inhibitor V

(2-Naphthylvinyl ketone; ZM 449829)

A breakdown product of JAK3 Inhibitor IV (**Cat. No. 420121**) that exhibits similar inhibitory potency (pIC_{50} = 6.8 for JAK3; 5.0 for EGFRK and 4.7 for JAK1). Also inhibits STAT-5 phosphorylation and T-cell proliferation. M.W. 182.2.



Cat. No. 420122 **10 mg** **$ 155**

New! MAP Kinase Research Tools

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

Purified, highly active, recombinant human MAP Kinase 1 (ERK1) produced by phosphorylation of the purified ERK1with MEK1. Suitable for labeling MAP Kinase substrates. Features a polyhistidine tag to facilitate removal of the enzyme from the reaction mixture. *Specific activity:≥6000 units/mg protein. Purity:≥95% by SDS-PAGE.*

Cat. No. 454849 **2.5 µg** **$ 250**

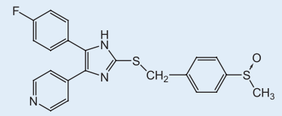
MAP Kinase 2, His•Tag®, Activated, Human, Recombinant, *E. coli.*

Purified, highly active, recombinant human MAP Kinase (ERK2) produced by phosphorylation of purified ERK2 with MEK1. Suitable for labeling MAP Kinase substrates. Features a polyhistidine tag to facilitate removal of the enzyme from the reaction mixture. *Specific activity: ≥5500 units/mg protein. Purity:≥95% by SDS-PAGE.*

Cat. No. 454854 **5 µg** **$ 250**

ML 3163

A cell-permeable 2-benzylsulfanyl imidazole that combines the structural features of cytokine release inhibitors SKF-86002 (**Cat. No. 567305**) and the p38 inhibitor SB 203580 (**Cat. No. 559389**). Blocks the release of TNF-α and IL-1β from human blood mononuclear cells (IC_{50} = 20.3 µM and 3.65 µM for TNF-α; 2.78 µM and 0.88 µM for IL-1β, respectively). Occupies the ATP binding site of p38 MAP kinase and inhibits its activity (IC_{50} = 4.0 µM). M.W.423.5



Cat. No. 475800 **1 mg** **$ 90**

Ref.: Laufer, S.A. and Wagner, G.K. 2002. *J. Med. Chem.* **45,** 2733

JNK2α2, His•Tag®, Human, Recombinant, *E. coli.*

Purified, active form of human JNK2α2 (SAPK1α), suitable for labeling JNK2α2 substrates. Features a polyhistidine tag to facilitate removal of the enzyme from the reaction mixture. *Specific activity:≥100 units/mg protein. Purity:≥95% by SDS-PAGE.*

Cat. No. 420124 **100 µg** **$ 295**

SB 239063

A potent inhibitor of p38α (IC_{50} = 44 nM for inhibition of recombinant purified human p38α). Blocks the production of IL-1 and TNF-α in LPS-stimulated human peripheral blood monocytes (IC_{50} = 120 and 350 nM, respectively). M.W. 368.4.

Cat. No. 559404 **500 µg** **$ 98**

ERK Activation Inhibitor Peptide I, Cell-Permeable

(Ste-MPKKKPTPIQLNP-NH_2)

A cell-permeable peptide corresponding to the N-terminal region of MEK1 that acts as a specific inhibitor of ERK activation and blocker of transcriptional activity of ELK1. Selectively binds to ERK2 and prevents its interaction with MEK (IC_{50} = 2.5 mM). Does not affect the activation of JNKs or p38. M.W. 3146.8.

Cat. No. 328000 **1 mg** **$ 120**

Ref.: Kelemen, B.R., et al. 2002. *J. Biol. Chem.* **277,** 8741.

ERK Activation Inhibitor Peptide II, Cell-Permeable

(H-GYGRKKRRQRRR-G-MPKKKPTPIQLNP-NH_2)

A peptide corresponding to the N-terminal region of MEK1 that is fused to the HIV-TAT membrane translocating peptide (MTP) sequence via a glycine linker. Acts as a specific inhibitor of ERK activation and blocks the transcriptional activity of ELK1. Binds to ERK2 and prevents its interaction with MEK (IC_{50} = 210 nM). Does not affect the activation of JNKs or p38. M.W. 3146.8.

Cat. No. 328005 **1 mg** **$ 160**

Ref.: Kelemen, B.R., et al. 2002. *J. Biol. Chem.* **277,** 8741.

New! Protein Prenylation Research Tools

FPTase, Rat, Recombinant, *E. coli*

A heterodimeric enzyme that catalyzes the transfer of a farnesyl group from farnesyl diphosphate to a variety of cellular proteins containing a C-terminal CaaX cysteine, thereby increasing the hydrophobicity of the protein. *Purity:≥90% by SDS-PAGE. M.W. α-subunit: ~48,000; β-subunit: ~46,000.*

Cat. No. 344145 **100 mg** **$ 280**

Ref.: Zimmerman, K.K., et al. 1998. *Protein Expr. Purif.* **14,** 395; Reiss, Y., et al. 1990. *Cell* **62,** 81.

GGTase Substrate, Fluorogenic (Dansyl-GCVLL)

A highly selective substrate for continuously monitoring GGTase-I activity (K_m = 5 µM) in the presence of geranylgeranyl diphosphate. S-Geranylgeranylation of the cysteine moiety results in a significant enhancement in fluorescence intensity (λ = 460 nm). *Purity:≥95% by HPLC. Excitation max.: ~360 nm; Emission max.: ~460 nm.*

Cat. No. 345845 **1 mg** **$ 70**

Ref.: Clausen, V.A., et al. 2001. *Biochemistry* **40,** 3920; Zhang, F.L., and Casey, P.J. 1996. *Biochem. J.* **320,** 925; Pickett, W.C., et al. 1995. *Anal. Biochem.* **225,** 60.

FTase Substrate, Fluorogenic (Dansyl-GCVLS)

A pentapeptide based on the carboxyl terminus of H-Ras with a dansyl group attached to the amino terminus. Serves as a highly selective substrate for continuously monitoring FTase activity (k_{cat} = 0.5 s^{-1}; K_m = 1.4 µM) in the presence of farnesyl diphosphate. S-Farnesylation of the cysteine results in about 13-fold enhancement in fluorescence intensity. *Excitation max.: ~340 nm; Emission max.: ~505 nm.* M.W. 710.9.

Cat. No. 344505 **1 mg** **$ 70**

Ref.: Bohm, M., et al. 2001. *J. Med. Chem.* **44,** 3117; Hightower, K.E., et al. 1998. *Biochemistry* **37,** 15555.

L-744,832

A potent, selective thiol-containing peptidomimetic farnesyltransferase (FTase) inhibitor that blocks p70s6k activation and DNA synthesis and promotes apoptosis. Induces expression of p21 and arrests cell cycle at G_1 phase. Shown to be effective against tumors that exhibit inappropriate activation of the mTOR/p70s6k pathway. M.W. 632.7

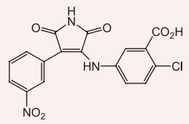
Cat. No. 422720 **5 mg** **$ 110**

Glycogen Synthase Kinase-3: Its Role in Neurodegenerative Disorders

Glycogen Synthase Kinase-3 (GSK-3; tau protein kinase I), a highly conserved, ubiquitously expressed serine/threonine protein kinase is involved in the signal transduction cascades of multiple cellular processes, including development, gene transcription, protein translation, cytoskeletal organization, cell cycle, and apoptosis. GSK-3 is negatively regulated by protein kinase B/Akt and by the Wnt signaling pathway. It exists in two isoforms, α and β. Higher levels of GSK-3β have been shown in pre-tangle and in phosphorylated tau bearing neurons. Overexpression of GSK-3β is a characteristic feature of Alzheimer's disease. GSK-3β accounts for most major phosphorylation sites of fetal and paired helical filament-tau. β-Amyloid peptides are shown to activate GSK-3β, suggesting that activation of GSK-3β is a key mechanism in pathogenesis of Alzheimer's disease. The development of GSK-3 inhibitors holds considerable promise for reducing tau phosphorylation and debilitating effects of Alzheimer's disease.

GSK-3 Inhibitor

A potent GSK-3 inhibitor (IC_{50} = 26 nM for GSK-3α) that does not affect the activity of over 20 other kinases including Cdk-2. M.W. 387.7.

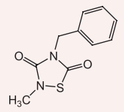


Cat. No. 361535 **1 mg** **$ 70**

Ref.: Smith, D.G., et al. 2001. *Bioorg. Med. Chem. Lett.* **11,** 635.

GSK-3β Inhibitor I (TDZD-8)

A highly selective, non-ATP competitive inhibitor of GSK-3β (IC_{50} = 2 μM). Binds to the active site of GSK-3β. Does not significantly affect the activities of Cdk-1/cyclin B, CK-II, PKA, or PKC (IC_{50} >100 μM). M.W. 222.3.

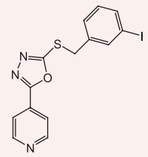


Cat. No. 361540 **5 mg** **$ 75**

Ref.: Martinez, A., et al. 2002. *J. Med. Chem.* **45,** 1292.

GSK-3 Inhibitor II

A 2-thio-[1,3,4]-oxadiazole-pyridyl derivative that acts as a potent inhibitor of GSK-3 (IC_{50} = 390 nM). M.W. 395.22.



Cat. No. 361541 **5 mg** **$ 80**

Ref.: Naerum, L., et al. 2002. *Bioorg. Med. Chem. Lett.* **12,** 1525.

Also Available ...

GSK-3β Substrates

GSK-3β Substrate (H-GPHRSTPESRAAV-OH)

A part of the hydrophilic loop domain of presenilin 1 that is selectively recognized by GSK-3β. The sequence is not recognized by p38α, p38β, PKC, CK-II. Undergoes phosphorylation at the Ser^{353} and Ser^{357} sites. M.W. 1364.5.

Cat. No. 361530 **1 mg** **$ 62**

Ref.: Kirschenbaum, F., et al. 2001. *J. Biol. Chem.* **276,** 7366.

GSK-3β Substrate, Negative Control (H-GPHRATPEARAAV-OH)

A negative control for GSK-3β Substrate (**Cat. No. 361530**) wherein the Ser^{353} and Ser^{357} are replaced with alanine residues. M.W. 1332.5.

Cat. No. 361531 **1 mg** **$ 62**

Ref.: Kirschenbaum, F., et al. 2001. *J. Biol. Chem.* **276,** 7366.

NEW! Antibodies for Alzheimer's Disease Research

Product	Cat. No.	Comments	Applications*	Size	Price
Anti-Nicastrin, C-Terminal (689-709), Human (Rabbit)	**481905**	Reacts with human and mouse and recognizes both the immature and mature forms of nicastrin.	IB, IP, RIA	100 μl	$ 280
Anti-Nicastrin, N-Terminal (62-93), Human (Rabbit)	**481906**	Reacts with human and mouse and recognizes both the immature and mature forms of nicastrin.	IB, IF, IP.	100 μl	280
Anti-Presenilin 1, Loop Domain (263-407), Human (Rabbit)	**529592**	Reacts with human, monkey, mouse, and rat and recognizes presenilin 1 holoprotein and its C-terminal fragments.	IB, IF, IP	100 μl	280
Anti-Presenilin 1, N-Terminal (1-65), Human (Rabbit)	**529591**	Reacts with human, monkey, mouse, and rat and recognizes presenilin 1 holoprotein and its N-terminal fragments.	IB, IF, IP	100 μl	280
Anti-Presenilin 2, Loop Domain (269-394), Human (Rabbit)	**529594**	Reacts with human and mouse and recognizes presenilin 2 holoprotein and its C-terminal fragments.	IB, IF, IP	100 μl	280
Anti-Presenilin 2, N-Terminal (1-75), Human (Rabbit)	**529593**	Reacts with human and mouse and recognizes presenilin 2 holoprotein and its N-terminal fragments.	IB, IF, IP	100 μl	280
Anti-Presenilin 2, Phospho-specific, ($Ser^{327/330}$), Human (Rabbit)	**529588**	Reacts with human and recognizes the ~23 kDa presenilin 2 phosphorylated at $Ser^{327/330}$.	IB	50 μg	245

* **IB**: Immunolotting; **IF**: Immunofluorescence; **IP**: Immunoprecipitation; **RIA**: Radioimmunoassay

New! Secretase Inhibitors and Substrates

Deposition of Aβ is an early event in the pathogenesis of AD. The β-amyloid gene, located on chromosome 21, encodes a transmembrane amyloid precursor protein (APP), which gives rise to Aβ. Processing and secretion of Aβ involves two cleavage steps. The first cleavage is carried out by β-secretase at Met^{671} of APP, creating a free amino terminus of Aβ (Asp^{672}). The second cleavage is achieved by γ-secretase at the C-terminal of Aβ (Aβ40 - 43). More recently, at least two distinct forms of γ-secretase have been reported, which exhibit either a γ-40 or a γ-42 activity. Inhibiting the activity of β- or γ-secretase is therapeutically attractive because clinical intervention at this step affects the early events that lead to plaque formation and neuronal death. CALBIOCHEM® introduces a wide selection of β- and γ-secretase inhibitors and substrates for your research needs.

β-Secretase Inhibitor III
(H-EVNstatine; Inhibitor GL189)

A substrate analog inhibitor of β-secretase (BACE) that blocks the proteolytic activity in solubilized membrane fractions from BACE transfected MDCK cells. M.W. 963.1.

Cat. No. 565780 **500 μg** **$ 85**

Ref.: Capell, A., et al. 2002. *J. Biol. Chem.* **277,** 5637; Tung, J.S., et al. 2002. *J. Med. Chem.* **45,** 259.

γ-Secretase Inhibitor XI
(7-Amino-4-Chloro-3-methoxyisocoumarin; JLK6)

An active site directed, irreversible inhibitor of γ-secretase that blocks the production of both $Aβ_{40}$ and $Aβ_{42}$ in HEK293 cells. M.W. 225.6.

Cat. No. 565772 **5 mg** **$ 90**

Ref.: Esler, W.P., et al. 2002. *Nat. Cell Biol.* **4,** E110; Petit, A., et al. 2001. *Nat. Cell Biol.* **3,** 507.

γ-Secretase Inhibitor XII (Z-IL-CHO)

A cell-permeable, reversible inhibitor of γ-secretase that blocks the production of both $Aβ_{40}$ and $Aβ_{42}$ (IC_{50} = 7.9 and 7.6 μM, respectively) and blocks the generation of CTF-γ. M.W. 362.5.

Cat. No. 565773 **5 mg** **$ 145**

Ref.: Weizen, S., et al. 2002. *Nat. Med.* **8,** 979.

γ-Secretase Inhibitor XIV [Z-C(*t*-Bu)-IL-CHO]

A cell-permeable, reversible inhibitor of γ-secretase that blocks the production of $Aβ_{40}$ and $Aβ_{42}$ (IC_{50} = 190 and 780 nM, respectively) *in vitro* as well as in CHO 2b-7 cells overexpressing APP695 (IC_{50} = 80 nM and 120 nM). M.W. 521.7.

Cat. No. 565777 **5 mg** **$ 88**

Ref.: McLendon, C., et al. 2000. *FASEB J.* **14,** 2383.

γ-Secretase Inhibitor XVI (DAPM)

A cell-permeable, highly potent inhibitor of γ-Secretase (IC_{50} = 10 nM in 7PA2 cells). Prevents early Aβ oligomerization by blocking Aβ dimer and trimer formation. M.W. 390.4

Cat. No. 565777 **5 mg** **$ 68**

Ref.: Walsh, D.M., et al. 2002. *Nature* **416,** 535.

γ-Secretase Inhibitor XVII

A cell-permeable (hydroxyethyl)urea peptidomimetic that acts as a transition-state analog inhibitor of γ-secretase (IC_{50} = 300 nM for Aβ production in whole cells). Binds the presenilin-γ-secretase complex (PS1-NTF, PS1-CTF, Nicastrin, and C83 APP CTF). Shown to inhibit the cleavage of N100Flag, a Notch-based substrate and C100Flag, an APP-based substrate in low nanomolar range. M.W. 640.8.

Cat. No. 565778 **500 μg** **$ 140**

Ref.: Kimberly, W.T., et al. 2002. *J. Biol. Chem.* **277,** 35113; Campbell, W.A., et al. 2002. *Biochemistry* **41,** 3372.

γ-Secretase Inhibitor XVIII

A cell-permeable peptidyl dihydrobenzodiazepinone derivative that acts as a highly potent, selective, non-transition state and non-competitive inhibitor of γ-secretase (IC_{50} $Aβ_{total}$= 300 pM in CHO cells overexpressing wild type βAPP). Binds to the active site of PS1 and PS2. M.W. 490.5.

Cat. No. 565779 **250 μg** **$ 135**

Ref.: Francis, R., et al. 2002. *Dev. Cell* **3,** 85; Tian, G., et al. 2002. *J Biol. Chem.* **277,** 31499; Lee, H.J., et al. 2002. *J. Biol. Chem.* **277,** 6318.

β-Secretase Substrate VI, Fluorogenic
[H-K(DABSYL0-SEVNLDAEFRQ(LY)]

A highly selective, fluorescence resonance energy transfer (FRET) peptide substrate for β-secretase (BACE; K_m = 9 μM). Derived from the Swedish mutant APP β-cleavage site.

Cat. No. 565781 **500 μg** **$ 255**

Ref.: Gruninger-leitch, F., et al. 2002. *J. Biol. Chem.* **277,** 4687.

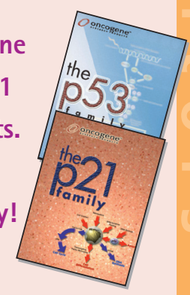
NEW! AROMATASE Inhibitor
(4-(Imidazolylmethyl)-1-nitro-9H-9-xanthenone)

A potent non-steroidal, selective, and competitive inhibitor of aromatase (P450arom; IC_{50} = 40 nM for human aromatase). Reported to be more potent than fadrozole in inhibiting aromatase activity.

Cat. No. 182540 **1 mg** **$ 95**

Ref.: Recanatini, M., et al. 2001. *J. Med. Chem.* **44,** 672.

Our complete line of p53 and p21 related products. Ask for your free copy today!

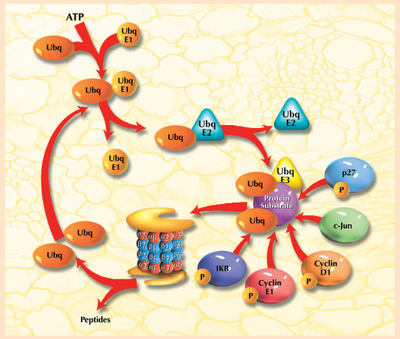


Looking for Novel β-Amyloid Precursor proteins?

Product	Cat. No.	Comments	Size	Price
β-Amyloid Precursor Protein, CTF-31, Synthetic	**171540**	A 31-amino acid peptide resulting from the cleavage of the C-terminus of β-APP at Asp^{739} and Ala^{740} by caspases.	250 μg	$ 130
β-Amyloid Precursor Protein, CTF-50, Synthetic	**171545**	A 50-amino acid peptide resulting from the γ-secretase cleavage of the C-terminus of β-APP at Leu^{720} and Val^{721}. May also serve as a precursor for C31, APP.	250 μg	180
β-Amyloid Precursor Protein, CTF-57, Synthetic	**171550**	A 57-amino acid peptide resulting from the γ-secretase cleavage of the C-terminus of β-APP at Ala^{713} and Thr^{714}.	250 μg	205

New! Protein Ubiquitination Research Tools

A vast majority of short-lived proteins are degraded by the ubiquitin-proteasome pathway. A protein marked for degradation is covalently attached to multiple molecules of ubiquitin, a highly conserved 76-amino acid (8.6 kDa) protein, by a multi-enzymatic system consisting of Ubiquitin-activating (E1), Ubiquitin-conjugating (E2), and the Ubiquitin-ligating (E3) enzymes. The E1 enzymes activate a Ubiquitin monomer at its C-terminal cysteine residue to a high-energy thiolester bond which is then transferred to a reactive cysteine residue of the E2 enzyme. The final transfer of ubiquitin to ε-amino group of a reactive lysine residue of substrate proteins is brought about by the E3 enzyme. Ubiquitinated protein is then escorted to the 26S proteasome where it undergoes final degradation and the ubiquitin is released and recycled.



New! Proteasome Inhibitors

Product	Cat. No.	Comments	Size	Price
AdaAhX$_3$L$_3$VS	**114802**	A potent, covalent, irreversible inhibitor of chymotrypsin-like (IC_{50} = 5 to 100 nM), trypsin-like (IC_{50} = 1 to 5 µM) and PGPH (IC_{50} = 0.5 - 1.0 µM) activities of the 20S proteasome.	250 µg	$ 185
AdaLys(Bio)AhX$_3$L$_3$VS	**114803**	A potent, covalent, biotinylated, irreversible inhibitor of chymotrypsin-like (IC_{50} = 5 to 100 nM), trypsin-like ((IC_{50} = 5.0 - 10.0 µM), and PGPH (IC_{50} = 2.0 - 5.0 µM) activities of the 20S proteasome. Useful for the detection of catalytic β subunits of constitutive proteasome and immunoproteasome through Western blotting.	250 µg	185
Proteasome Inhibitor IV	**539175**	A highly selective, potent proteasomal inhibitor (K_is = 1.5 µM for branched chain amino acid preferring, 2.3 µM for small neutral amino acid preferring, and 40.5 µM for chymotrypsin-like activities; IC_{50} = 3.1 mM for peptidylglutamyl-peptide hydrolyzing activity).	5 mg	155
Tyropeptin A, Synthetic	**657008**	A cell-permeable peptide aldehyde that acts as a highly selective, competitive, reversible inhibitor of chymotrypsin-like activity of 20S proteasome (IC_{50} = 100 ng/ml). Does not affect peptidylglutamyl-peptide hydrolyzing (PGPH)-like activity even at 100 mg/ml. Inhibits α-chymotrypsin, cathepsin L and m-calpain (IC_{50} = 720 ng/ml, 190 ng/ml and 740 ng/ml, respectively).	1 mg 5 mg	55 215

Ubiquitin Conjugating Enzyme Set

Set contains 10 µg each of the following ubiquitin conjugating (E2) enzymes: GST-Tagged UbcH2 (**Cat. No. 662111**), His•Tag® UbcH3, GST-Tagged UbcH5a (**Cat. No. 662091**), GST-Tagged UbcH5b (**Cat. No. 662092**), GST-Tagged UbcH5c (**Cat. No. 662093**), His•Tag® UbcH6 (**Cat. No. 662094**), UbcH7, and His•Tag® UbcH10 (**Cat. No. 662095**).

Cat. No. 662116 **1 Set** **$ 475**

Ubiquitin Conjugating Enzyme Active Site Mutants Set

Set contains 10 µg each of the following ubiquitin conjugating (E2) enzymes mutated at the active site from cysteine to serine: GST-Tagged UbcH5a (**Cat. No. 662112**), His•Tag® UbcH6 (**Cat. No. 662113**), UbcH7 (**Cat. No. 662114**), and His•Tag® UbcH10 (**Cat. No. 662115**).

Cat. No. 662117 **1 Set** **$ 275**

Ubiquitinated Protein Enrichment Kit

A kit for rapidly isolating and enriching ubiquitinated proteins (UbP) from a variety of samples. Employs affinity beads comprised of a GST fusion protein containing a ubiquitin-associated sequence conjugated to glutathione-agarose. The UbP can be identified by loading the beads directly onto SDS-PAGE and then immunoblotting with Anti-Ubiquitin (**Cat. No. 662099**). Beads can also be treated with Isopeptidase T (**Cat. No. 419700**) to release the proteins from the ubiquitin chains. Each kit is sufficient to process 12.5 - 25 mg lysate.

Cat. No. 662200 **1 kit** **$ 295**

Human Proteasome Isolation Kit

A kit for isolation of biologically active proteasomes using affinity matrix beads comprised of a GST-fusion protein containing an ubiquitin-like domain (UbL) bound to GST-agarose. The proteasome subunit proteins can be identified by loading the beads directly onto an SDS-PAGE gel and immunoblotting with subunit specific antibodies. Alternatively, proteasome bound to beads can be used in proteolytic assays using proteasome substrates. Each kit is sufficient to process 12.5 to 25 mg of lysate.

Cat. No. 539176 **1 kit** **$ 325**

Enzymes and Regulatory Proteins for the Ubiquitin-Proteasome Pathway

Nedd8, Human, Recombinant

Cat. No. 480020 **1 mg** **$ 295**

Nedd8 Precursor, Human, Recombinant (Pro-Nedd8)

Cat. No. 480021 **1 mg** **$ 295**

SUMO-1, GST-Tagged, Human, Recombinant (Sentrin)

Cat. No. 574400 **1 mg** **$ 265**

Ubiquitin Conjugating Enzyme 2, GST-Tagged, Human, Recombinant, *E. coli*

Cat. No. 662111 **50 µg** **$ 195**

Ubiquitin Conjugating Enzyme 5a, Active Site Mutant, GST-Tagged, Human, Recombinant, *E. coli*

(UbcH5a active site mutant)

Cat. No. 662112 **50 µg** **$ 195**

Ubiquitin Conjugating Enzyme 6, Active Site Mutant, His•Tag®, Human, Recombinant, *E. coli*

(UbcH6 active site mutant)

Cat. No. 662113 **50 µg** **$ 195**

Ubiquitin Conjugating Enzyme 7, Active Site Mutant, Human, Recombinant, *E. coli*

(UbcH7 active site mutant)

Cat. No. 662114 **50 µg** **$ 195**

Ubiquitin Conjugating Enzyme 10, Active Site Mutant, His•Tag®, Human, Recombinant, *E. coli*

(UbcH10 active site mutant)

Cat. No. 662115 **50 µg** **$ 195**

NEW! Anthrax Lethal Factor Substrates and Inhibitors

Anthrax LF Protease Substrate, Fluorogenic

An internally-quenched fluorogenic 19-mer peptide substrate derived from the MAP kinase kinase (MEK) substrate motif. Acts as a sensitive substrate for rapid monitoring of Anthrax Lethal Factor (LF) protease activity.

Cat. No. 176902 **500 mg** **$ 275**

Ref.: Cummings, R.T., et al. 2002. *Proc. Natl. Acad. Sci. USA* **99,** 6603.

Anthrax LF Protease Substrate II, Colorimetric

(Ac-GYbARRRRRRRRVLR*p*NA)

An N-acetylated, C-*p*-nitroanilide (pNA) derivative of a 14-mer peptide substrate designed from MEK-2 template that is useful for measuring Anthrax lethal factor (LF) metalloproteolytic activity with a detection limit of ~100 pM. The release of pNA is monitored by recording the absorption at ~405 nm. Useful for high-throughput screening of LF inhibitors.

Cat. No. 176903 **1 mg** **$ 165**

Ref.: Tonello, F., et. al. 2002. *Nature* **418,** 386.

Anthrax LF Protease Substrate III, Fluorogenic

(Ac-GYbARRRRRRRRVLRAMC)

An N-acetylated, AMC derivative of a 14-mer peptide substrate designed from MEK-2 template that is useful for measuring Anthrax lethal factor (LF) metalloproteolytic activity with a detection limit of ~5 - 10 pM. Useful for high-throughput screening of LF inhibitors.

Cat. No. 176904 **1 mg** **$ 175**

Ref.: Tonello, F., et. al. 2002. *Nature* **418,** 386.

Anthrax LF Protease Inhibitor

(Ac-GYbAlaRRRRRRRRVLRNHOH)

A cell-permeable N-acetylated, C-hydroxamate derivative of a 14-mer peptide designed from MEK-2 template that acts as a competitive inhibitor of Anthrax lethal factor metalloproteinase (K_i = 1 nM). Also inhibits MEK-3 cleavage. Shown to protect against Anthrax toxin induced cytotoxicity in RAW264.7 and J772.A1 cells.

Cat. No. 176901 **1 mg** **$ 175**

Ref.: Tonello, F., et. al. 2002. *Nature* **418,** 386.

Involved in Osteoporosis Research? Try our NEW Inhibitors of Bone Resorption...

Alendronate, Sodium Salt

Metal ion chelator that acts as a potent inhibitor of bone resorption and cartilage destruction. Induces apoptosis in osteoclast and macrophages by inhibiting farnesyl diphosphate synthase (IC_{50} = 460 nM). M.W. 325.1.

Cat. No. 126855 **100 mg** **$ 124**

Clodronate, Dosodium Salt

A metal chelator that acts as an inhibitor of osteoclast-mediated bone resorption and induces apoptosis by inhibiting mitochondrial functions. M.W. 360.9.

Cat. No. 233183 **10 mg** **$ 72**

Pamidronate, Disodium Salt

A potent inhibitor of osteolysis that blocks tumor-induced osteolysis. Reported to inhibit the cell growth and induce apoptosis in human melanoma cells *in vitro*. M.W. 279.0.

Cat. No. 506600 **10 mg** **$ 70**

p53: Choice of Response – Repair or Death

p53, a phosphoprotein of about 390 amino acids consists of four domains: a highly charged acidic region of about 75 to 80 residues, a hydrophobic proline-rich domain (position 80 to 150), a central region (from 150 to about 300), and a highly basic C-terminal region. p53 is phosphorylated at many sites by stress-activated protein kinases, DNA Protein kinase, casein kinase I and II, and cyclin-dependent kinases. When normal mammalian cells are subjected to stress signals (e.g. hypoxia, radiation, chemotherapeutic drugs) p53 is activated and its ubiquitin-dependent degradation is blocked. The resulting increase in p53-dependent gene transcription leads to the p53-mediated induction of programmed cell death and/or cell cycle arrest. Activation of p53 can result in cell cycle arrest, presumably to allow for DNA repair to occur before replication or mitosis. In some cell types, however, p53 activation results in apoptosis as means of eliminating irreparably damaged cells. The final outcome of p53 activation depends on many factors, and is mediated largely through the action of downstream effectors genes transactivated by p53. Functional p53 is thought to provide a protective effect against tumor growth. Since radiotherapy and chemotherapy act in part by triggering cell suicide in response to DNA damage, the function of p53 is critical to the way that many cancer treatments kill cells. A successful response to therapy is greatly reduced in tumors where mutant p53 is present and these tumors are often very difficult to treat.

p53, Wild-Type, Recombinant

Expressed in baculovirus system. *Activity: 1.0 unit/ng of protein. One unit is sufficient for a gel mobility assay in a 20 µl reaction; 50 units are sufficient for reconstituted transcription assay and 100 units are sufficient for a protein-protein interaction assay. Purity: ≥95% by SDS-PAGE.*

Cat. No. 506147 5000 Units $ 525

p53 (1-342, C-Terminal Deletion), Recombinant

Expressed in baculovirus system. A p53 mutant protein (amino acids 1 - 342) with deletion of 51 residues at the C-terminal, including the entire basic domain and part of tetramerization domain. The tetramerization domain of p53 plays an important role in cell cycle. Disruption or loss of oligomerization function is associated with loss of cell cycle arrest. This mutant protein can be used as a unique tool to study specific function of p53 related to the C-terminus. *One unit is sufficient for a gel mobility assay in a 20 µl reaction; 50 units are sufficient for reconstituted transcription assay and 100 units are sufficient for a protein-protein interaction assay. Purity: ≥95% by SDS-PAGE.*

Cat. No. 506146 5000 Units $ 525

PRIMA-1

(**p**53 **r**eactivation and **i**nduction of **m**assive **a**poptosis)

A cell-permeable quinuclidinone analog with antitumor properties. Induces p53-dependent apoptosis in human tumor cells through restoration of the transcriptional transactivation function to mutant p53. Restores sequence-specific DNA binding and the active conformation to mutant p53 proteins. It suppresses tumor growth in mice with no apparent toxicity. M.W. 185.2.

Cat. No. 530050 10 mg $ 85

Ref.: Bykov, V.J., et al. 2002. *Nat. Med.* **8,** 282.

Looking for Caspases?

Caspase-3, Mouse, Recombinant, *E. coli*

Cat. No. 235414 100 Units $ 295

Caspase-3, Rat, Recombinant, *E. coli*

Cat. No. 235415 100 Units $ 295

Procaspase-3, Mouse, Recombinant, *E. coli*

Cat. No. 529662 5 µg $ 330

Procaspase-7, Human, Recombinant, *E. coli*

Cat. No. 529665 5 µg $ 390

Procaspase-3, Human, Recombinant, *E. coli*

Cat. No. 529670 5 µg $ 390

For Convenience and Economy

Caspase Enzymes Set, Group I

Contains 25 units each of Caspase-1, 4, and 5

Cat. No. 218816 1 Set $ 380

Caspase Enzymes Set, Group II

Contains 25 units each of Caspase-2, 3, and 7

Cat. No. 218817 1 Set $ 380

Caspase Enzymes Set, Group III

Contains 25 units each of Caspase-6, 8, 9, and 10

Cat. No. 2188196 1 Set $ 475

New! Inhibitors for Apoptosis Research

Midkine, Human, Recombinant, *E. coli*

A member of the heparin-binding neurotrophic factor family that promotes neurite extension and neuronal survival. Shown to inhibit apoptosis by suppressing the activation of caspase-3 through the ERK cascade. M.W. 13,400.

Cat. No. 475833 5 µg $ 185

Ref.: Owada, K., et al. 1999. *J. Neurochem.* **73,** 2084; Asia, T., et al. 1997. *Biochem. Biophys. Res. Commun.* **236,** 66; Kovesdi, I., et al.1990. *Biochem. Biophys. Res. Commun.* **172,** 850.

Apoptosis Inhibitor (2,2′-Methylenebis(1,3-cyclohexanedione)

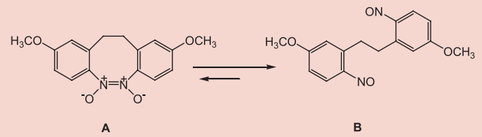
A cell-permeable, apoptosis induction inhibitor (IC_{50} = 67 mg/ml in FasL-stimulated WC8 cells, 130 mg/ml in etoposide-stimulated U937 cells). The anti-apoptotic effects are attributable to the inhibition of caspase-3 activation (IC_{50} = 79 mg/ml in etoposide-stimulated U937 cells). Does not affect the activity of caspase-3 even at 1 mg/ml. M.W. 236.3.

Cat. No. 178488 10 mg $ 85

Ref.: Tsuda, T., et al. 2001. *Eur. J. Pharmacol.* **433,** 37.

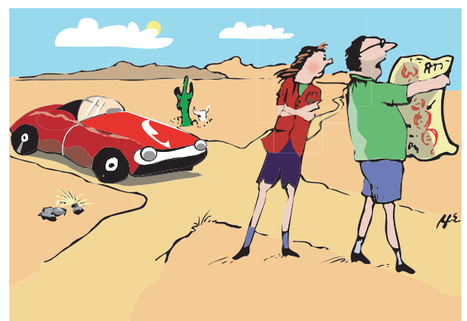
Bcl-2 Inhibitor

Contains a mixture of two tautomers (A and B) blocks the binding of the Bak BH3 peptide to Bcl-2 *in vitro* (IC_{50} = 10 µM). Inhibits cell viability and growth in HL-60 cells with high Bcl-2 expression (IC_{50} = 4 µM). Induces apoptosis in only those cancer cells that exhibit high Bcl-2 expression with minimal effect on cells with low Bcl-2 expression.



Cat. No. 197330 5 mg $ 145

Ref.: Enyedy, I.J., et al. 2001. *J. Med. Chem.* **44,** 4313.



"We're not lost. Here's a map of the human genome!"

NEW! Oxidative Stress Research Tools

Rosmarinic Acid

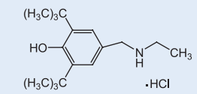
A naturally-occurring compound with antioxidant and anti-inflammatory properties. Inhibits microsomal lipid peroxidation by 90% at a concentration of 25 mg/ml. Blocks complement activation by reacting with the activated thioester of metastable C3b, which results in covalent attachment of the inhibitor to protein. *Purity: ≥98% by HPLC.* M.W. 360.3.

Cat. No. 557365 5 mg $ 47

Ref.: Sahu, A., et al. 1999. *Biochem. Pharmacol.* **57,** 1439; Liu, G.-T., et al. 1992. *Biochem. Pharmacol.* **43,** 147.

LY 231617

A potent antioxidant that readily crosses the blood-brain barrier and significantly reduces ischemia-induced or hydrogen peroxide-induced neuronal damage and inhibits lipid peroxidation (IC_{50} = 22 µM). Reported to block nuclear translocation of activated NF-κB in hippocampal neurons. *Purity: ≥95% by HPLC.* M.W. 299.9.

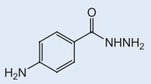


Cat. No. 440208 5 mg $ 135

Ref.: Fuson, K.S., et al. 1999. *J. Neurochem.* **72,** 1154; O'Neill, M.J., et al. 1997. *Brain Res.* **760,** 170; Clemens, J.A., et al. 1993. *Stroke* **24,** 716.

Myeloperoxidase Inhibitor- I

A benzoic acid hydrazide analog that acts as a potent, irreversible, and specific inhibitor of the peroxidation activity of myeloperoxidase (MPO; IC_{50} = 300 nM). Does not inhibit catalase or glutathione peroxidase activities. Shown to inhibit H_2O_2-induced apoptosis in HL-60, human leukemia cells. *Purity: ≥98% by HPLC.* M.W. 151.2



Cat. No. 475944 1 g $ 43

Ref.: Engelmann, I., et al. 2000. *Redox Report* **5,** 207; Wagner, B.A., et al. 2000. *J. Biol. Chem.* **275,** 22461; Burner, U., et al. 1999. *J. Biol. Chem.* **274,** 9494.

Cytochrome P450 1B1 Inhibitor, TMS

((E)-2,3′,4,5′-Tetramethoxystilbene)

A cell-permeable, potent, selective competitive inhibitor of cytochrome P450 1B1 (IC_{50} = 6 nM for cytochrome P450 1B1, 300 nM for cytochrome P450 1A1 and 3.1 µM for cytochrome P450 1A2). Reversibly binds to the heme region of P450 1B1 (K_d = 3 µM).

Cat. No. 250330 1 mg $ 125

Ref.: Kim, S., et al. 2002. *J. Med. Chem.* **45,** 160; Chun, Y.J., et al. 2001. *Cancer Res.* **61,** 8164.

Antibodies to Various Calpain Domains

Product	Cat. No.	Comments	Applications*	Size	Price
Anti-Calpain-1, C-Terminal, Human (Rabbit)	**208753**	Reacts with ~80 kDa latent and ~58 kDa active form of Calpain -1 in human, mouse, and rat. Does not react with other calpains.	IB	100 µg	$ 265
Anti-Calpain-1, Domain I, Human (Rabbit)	**208751**	Reacts with ~80 kDa latent and ~58 kDa active form of Calpain -1 in human, mouse, and rat. Does not react with other calpains.	IB	100 µg	265
Anti-Calpain-1, Domain II, Bovine (Mouse)	**208727**	Epitope lies within amino acids 245-265 of human calpain-1. Reacts with bovine, human, and rat.	IB, IF	100 µl	281
Anti-Calpain-1, Domain III, Bovine (Mouse)	**208728**	Epitope lies within amino acids 465-520 of human calpain-1. Reacts with bovine, human, porcine, and rat.	IB, IC	100 µl	281
Anti-Calpain-1, Domain IV, Human (Rabbit)	**208752**	Reacts with ~80 kDa latent and ~58 kDa active form of Calpain -1 in human, mouse, and rat. Does not react with other calpains.	IB	100 µg	265
Anti-Calpain, Large Subunit, Human (Rabbit)	**208732**	Does not cross-react with small subunit of calpain-1. Reacts with human.	IB	100 µl	206
Anti-Calpain-1/2, Small Subunit, Human Placenta (Mouse)	**208730**	Reacts with both native and denatured forms of 30 kDa subunit of calpain-1 in bovine and human.	ELISA, IB, IP	100 µg	265
Anti-Calpain-2, Domain I, Human (Rabbit)	**208754**	Reacts with ~80 kDa latent calpain-2 in human, mouse, and rat. Does not recognize ~58 kDa amino terminal processed active calpain-2.		100 µg	265
Anti-Calpain-2, Domain III, Human (Rabbit)	**208755**	Reacts with ~80 kDa latent and ~58 kDa active forms of calpain-2 in human, mouse, and rat.	IB	100 µg	265
Anti-Calpain-2, Domain III, Rat (Rabbit)	**208737**	Reacts with ~80 kDa latent and ~58 kDa active forms of calpain-2 in rat.	IB	100 µg	280
Anti-Calpain-2, Domain III/IV, Bovine (Mouse)	**208729**	Epitope lies within amino acids 502-699 of calpain-2. Reacts with bovine, human, and rat.	IB, IF	100 µg	265
Anti-Calpain-2, Domain IV, Human (Rabbit)	**208756**	Reacts with ~80 kDa latent and ~58 kDa active forms of calpain-2 in human, mouse, and rat.	IB	100 µg	265
Anti-Calpain-3, Domain I, Human (Rabbit)	**208757**	Reacts with ~94 kDa latent and ~62 kDa active forms of calpain-3 and with 82 kDa and 60 kDa cleavage products in human muscle.	IB	100 µg	265
Anti-Calpain-3, Domain III (Insert #1), Human (Rabbit)	**208758**	Reacts with ~94 kDa latent and ~62 kDa active forms of calpain-3 and with 82 kDa and 60 kDa cleavage products in human muscle.	IB	100 µg	265
Anti-Calpain-3, Domain III (Insert #2), Human (Rabbit)	**208759**	Reacts with ~94 kDa latent and ~62 kDa active forms of calpain-3 and with 82 kDa and 60 kDa cleavage products in human muscle.	IB	100 µg	265
Anti-Calpain-5, Domain I, Human (Rabbit)	**208760**	Reacts with ~73 kDa latent calpain-5 and with several smaller bands of calpain-5 cleaved at the carboxy terminus in human, mouse, and rat.	IB	100 µg	265
Anti-Calpain-5, Domain II, Human (Rabbit)	**208761**	Reacts with ~73 kDa latent and ~58 kDa active calpain-5 and with several smaller cleavage products of calpain-5 in human, mouse, and rat.	IB	100 µg	265
Anti-Calpain-5, Domain III, Human (Rabbit)	**208762**	Reacts with ~73 kDa latent and ~58 kDa active calpain-5 and with several smaller cleavage products of calpain-5 in human, mouse, and rat.	IB	100 µg	265
Anti-Calpain-5, Domain T, Human (Rabbit)	**208763**	Reacts with ~73 kDa latent and ~58 kDa active calpain-5 and with several smaller cleavage products of calpain-5 in human, mouse, and rat.	IB	100 µg	265
Anti-Calpain-6, Domain I, Human (Rabbit)	**208764**	Reacts with ~75 kDa latent and ~58 kDa active calpain-6 and with several smaller cleavage products of calpain-6 in human, mouse, and rat.	IB	100 µg	265
Anti-Calpain-6, Domain II, Human (Rabbit)	**208765**	Reacts with ~75 kDa latent and ~58 kDa active calpain-6 and with several smaller cleavage products of calpain-6 in human, mouse, and rat.	IB	100 µg	265
Anti-Calpain-6, Domain T, Human (Rabbit)	**208766**	Reacts with ~75 kDa latent and ~58 kDa active calpain-6 and with several smaller cleavage products of calpain-6 in human, mouse, and rat.	IB	100 µg	265
Anti-Calpain-7, Propeptide Domain I, Human (Rabbit)	**208767**	Reacts with ~93 kDa latent form of calpain-7 in human, mouse, and rat.	IB	100 µg	265
Anti-Calpain-7, Domain N, Human (Rabbit)	**208768**	Reacts with ~93 kDa latent and ~58 kDa form of calpain-7 in human, mouse, and rat.	IB	100 µg	265
Anti-Calpain LP82/LP85, Rat (Rabbit)	**208738**	Recognizes the latent large subunits of lens specific LP82 and LP85 and the ~62 kDa active LP85.	IB	100 µg	258
Anti-Calpain LP85, Rat (Rabbit)	**208739**	Recognizes the latent large subunits and the active ~62 kDa lens specific LP85 in rat.	IB	100 µg	258

* **ELISA**: Enzyme-linked Immunosorbent Assay; **IB**: Immunolotting; **IF**: Immunofluorescence; **IP**: Immunoprecipitation

Convenience, Consistency, and Reliability of Kits...

Phosphoprotein Enrichment Kit

Suitable for enrichment of phosphoproteins from tissues or cell culture for Western blotting. Kit contains columns, wash buffer, elution buffer, lysis buffer, SDS-PAGE sample buffer, and a directional insert. Sufficient to process up to 80 mg of phosphoprotein.

Cat. No. 525278 **1 kit** **$ 411**

Akt Activity Assay Kit

Non-radioactive assay kit for Akt activity in cell or tissue lysates. Contains kinase extraction buffer, Akt antibody, protein A agarose, GSK-3α protein/ATP mixture, kinase assay buffer, GSK-3α, phospho-specific antibody, and a directional insert.

Cat. No. 124007 **1 kit** **$ 475**

LCAT Activity Assay kit, Fluorometric

For quantitative assay of lecithin:cholesterol acyltransferase activity in human plasma. Includes LCAT substate, READ reagent, and a directional insert.

Cat. No. 428900 **1 Kit** **$ 350**

Histone Deacetylase Activity Assay Kit, Colorimetric

A two-step assay for HDAC activity in cell extracts. Includes substrate, assay buffer, lysine developer, HDAC inhibitor, HeLa cell nuclear extract positive control, deacetylated substrate standard, and a directional insert.

Cat. No. 382166 **1 Kit** **$ 350**

Histone Deacetylase Activity Assay Kit, Fluorometric

A two-step assay for HDAC activity in cell extracts. Includes substrate, assay buffer, lysine developer, HDAC inhibitor, HeLa cell nuclear extract positive control, deacetylated substrate standard, and a directional insert.

Cat. No. 382167 **1 Kit** **$ 330**

Cyclooxygenase Inhibitors

New! COX-2 Inhibitor I (LM-1685)

A potent and selective inhibitor of COX-2 (IC_{50} = 650 nM vs 10 µM for COX-1).

Cat. No. 236011 **5 mg** **$ 160**

Ref.: Palomer, A., et al. 2002. *J. Med. Chem.* **45,** 1402.

New! Cyclooxygenase Inhibitor Set

Contains		
Meloxicam (**Cat. No. 444800**)	10 mg	COX-2>COX-1
NS-398 (**Cat. No. 349254**)	5 mg	COX-2
SC-560 (**Cat. No. 565610**)	5 mg	COX-1
Sulindac Sulfide (**Cat. No. 574102**)	5 mg	COX-1

Cat. No. 239783 **1 Set** **$ 291**

Singlet Oxygen Donors

DHPN (N,N′-di(2,3-Dihydroxypropyl)-1,4-naphthalenedipropanamide)

Forms an endoperoxide ($DHPNO_2$) in the presence of singlet oxygen ($^1O_2$) whose thermal decomposition in the cell serves as the intracellular chemical source of 1O2.

Cat. No. 265675 **20 mg** **$ 125**

NDP (3,3′-(1,4-Naphthylidine)dipropionate, 2Na)

Forms an endoperoxide ($NDPO_2$) in the presence of singlet oxygen ($^1O_2$) whose thermal decomposition serves as an extracellular chemical source of $^1O_2$.

Cat. No. 479980 **20 mg** **$ 114**

NEW! Protein Synthesis Research Tools

Product	Cat. No.	Comments	Size	Price
Ebulin 1, *Sambucuc ebulus* L.	**324490**	Blocks protein synthesis by inactivating mammalian ribosomes.	1 mg	$ 291
eIF-4E, Human, Recombinant, *E. coli*	**324882**	An mRNA cap-binding protein involved in the rate limiting step of protein synthesis.	1 µg	225
eIF-4ES^{209A}, Human, Recombinant, *E. coli*	**324883**	Recombinat eIF-4E mutant at the Ser^{209} phosphorylation site to alanine.	1 µg	225
eIF-4ES^{209A}, Human, Recombinant, *E. coli*	**324884**	Recombinat eIF-4E mutated at the Thr^{210A} phosphorylation site to alanine.	1 µg	225
eIF-4ES^{209A}/T^{210A}, Human, Recombinant, *E. coli*	**324885**	Recombinat eIF-4E doubly mutated at Ser^{209} and Thr^{210} phosphorylation sites to alanine.	1 µg	225
eIF-4E^{S53A}, Human, Recombinant, *E. coli*	**324886**	Recombinat eIF-4E mutant at the Ser^{209} phospho-rylation site to alanine.	1 µg	225
Nigrin β, *Sambucus nigra* L.	**481991**	Blocks mammalian protein synthesis by inactivating ribosomes	1 mg	291

Antibodies to Cathepsins

Product	Cat. No.	Comments	Applications	Size	Price
Anti-Cathepsin F, Human (Rabbit)	**219359**	Detects ~32 kDa cathepsin F in human and mouse.	IB	100 µl	$ 225
Anti-Cathepsin Z, Human (Rabbit)	**219378**	Detects ~35 kDa cathepsin Z in human.	IB	100 µl	225