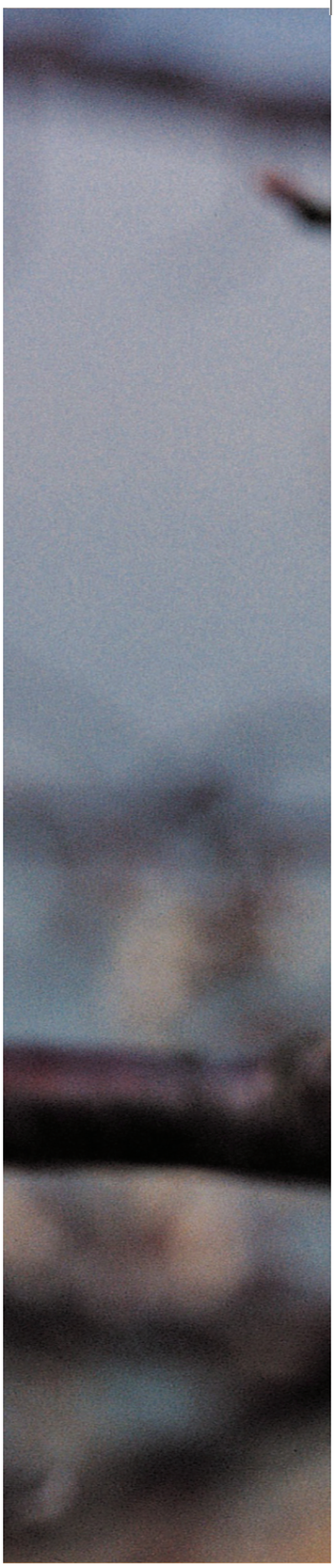

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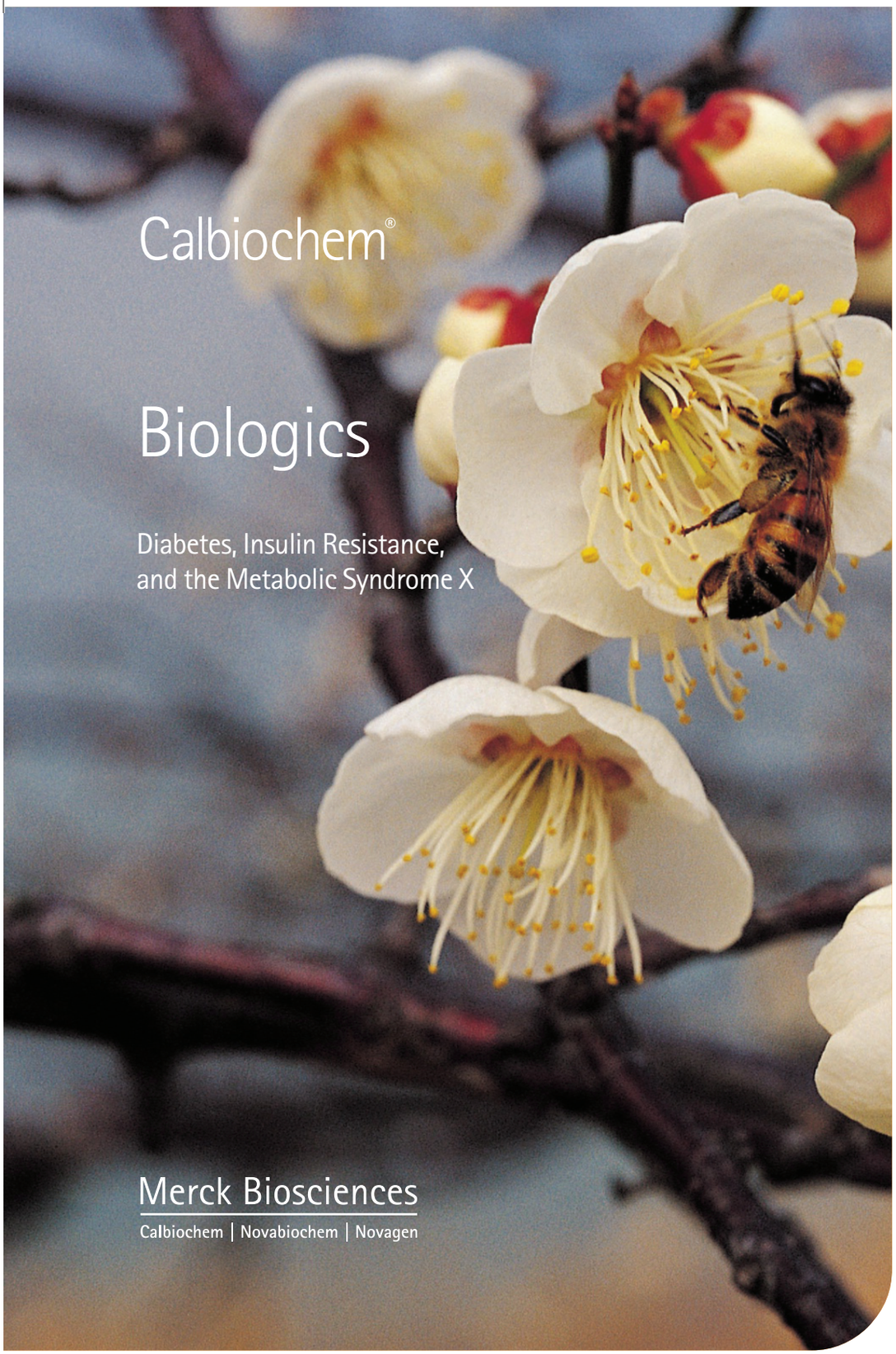

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Diabetes, Insulin Resistance, and the Metabolic Syndrome X

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Volume 32, No. 2, 2006

Inside this Issue...

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Diabetes, Insulin Resistance, and the Metabolic Syndrome X

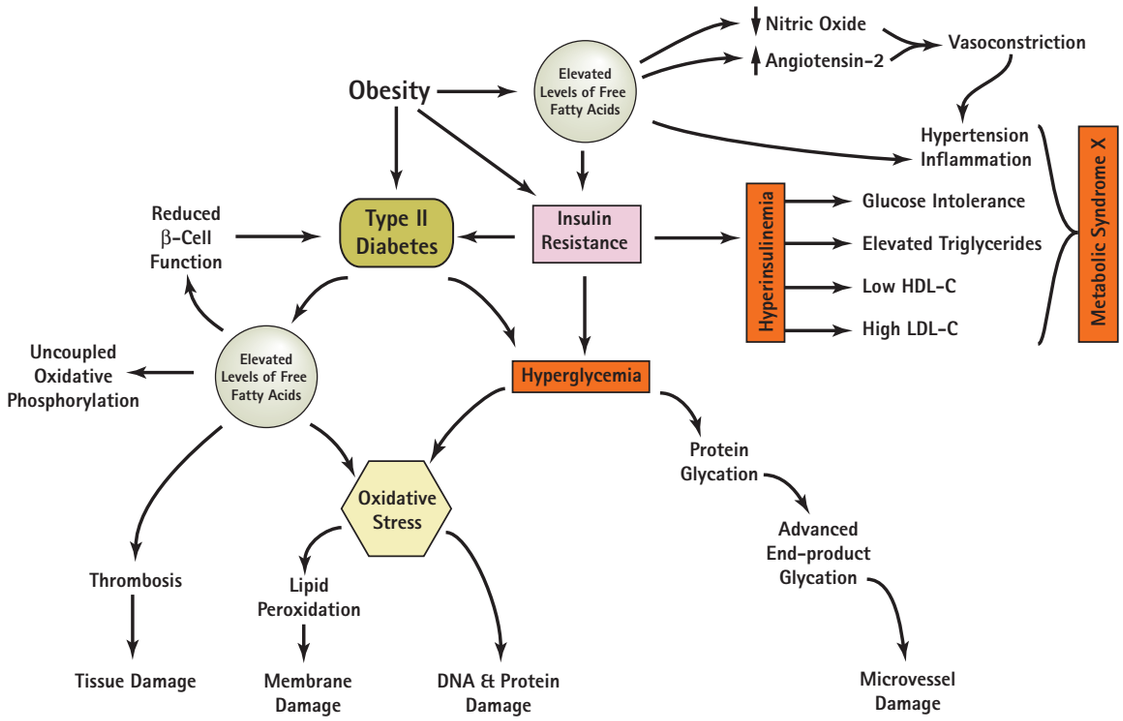
Chandra Mohan, Ph.D., Merck Biosciences

Diabetes is a chronic metabolic disorder that affects about 5% of the population in industrialized nations and accounts for over $100 billion in medical costs. Type l diabetes often manifests in childhood and may result from autoimmune destruction of β-cells. Type II diabetes, a more widespread metabolic disorder, generally manifests after the age of 40 and involves progressive development of insulin resistance leading to overt hyperglycemia. Insulin is the major hormone that counters the concerted action of a number of hyperglycemia-generating hormones. It enhances glucose uptake in muscle and adipose tissue, and reduces gluconeogenesis and lipolysis. Insulin resistance, caused by obesity, can result in elevated fasting and postprandial glucose levels and predispose individuals to the risk of type II diabetes.

Action of insulin on target cells is mediated via its interaction with insulin receptor (IR), a heterotetrameric glycoprotein consisting of two extracellular α-subunits (135 kDa) and two transmembrane β-subunits (95 kDa). IR functions as an allosteric enzyme in which the α-subunit inhibits the tyrosine kinase activity of the β-subunit. Insulin binding to the α-subunits results in the stimulation of the tyrosine kinase activity of the β-subunits. The kinase domains of the β-subunits are juxtaposed to the α-subunits, which permit autophosphorylation of Tyr^{1158}, Tyr^{1162}, and Tyr^{1163}, the first step in receptor activation. IR transphosphorylates tyrosine residues on several immediate substrates including insulin receptor substrate (IRS) proteins 1-4, Shc, Grb-2 associated binder-1 (Gab1), and APS adapter protein, all of which provide specific docking sites for other signaling proteins containing SH2 domains. These events lead to the activation of downstream signaling molecules, including PI 3-kinase (PI 3-K). The four IRS proteins exhibit a high degree of homology. IRS-1-knockout mice exhibit growth retardation and impaired glucose tolerance due to resistance to insulin and insulin-like growth factor-1 (IGF-1). IRS-2-knockout mice show severe insulin resistance in the liver and peripheral tissues and develop overt type II diabetes. In addition to tyrosine phosphorylation, both IR and IRS proteins undergo serine phosphorylation by PKC, GSK-3, Akt, and mTOR, which attenuate insulin signaling by blocking insulin-stimulated tyrosine phosphorylation. This serves as a negative feedback loop for insulin signal transduction and allows crosstalk with other pathways that may mediate insulin resistance. Recently, inhibitors of PI 3-K were shown to block the degradation of IRS-1 and the insulin-stimulated increase in Ser^{312} phosphorylation.

PI 3-K plays a critical role in the metabolic actions of insulin. Inhibitors of class Ia PI 3-K, such as LY 294002, or transfections with dominant negative constructs of the enzyme, block most metabolic actions of insulin, including stimulation of glucose transport, and glycogen and lipid synthesis. Activated PI 3-K specifically phosphorylates PI substrates generating PIP_2 and PIP_3, which then enlist PI 3-K-dependent kinase (PDK1) and Akt from the cytoplasm to the plasma membrane. This leads to conformational changes in Akt, allowing it to be phosphorylated on Thr^{308} and Ser^{473} by PDK1 and PDK2, respectively, to achieve full activation. Akt phosphorylates GSK-3 and inactivates it, which then allows the activation of glycogen synthase to proceed. Activation of Akt also results in the translocation of GLUT4 vesicles to the cell membrane where they participate in the transport of glucose.

Insulin resistance observed in obesity and type II diabetes is characterized by defects at many levels, including decreases in the number of insulin receptors and their tyrosine kinase activity, the concentration and phosphorylation of IRS-1 and -2, PI 3-K activity, and an impairment in insulin-stimulated recruitment of GLUT4 transporter from its intracellular storage compartment to the cell surface. These abnormalities result in a variety of metabolic defects, including hyperglycemia, hyperlipidemia, and hyperinsulinemia. Adipose tissue plays a vital role in the development of insulin resistance and associated abnormalities. A higher circulating level of free fatty acids (FFA), as observed in obesity and type II diabetes, is considered to be an important contributor to insulin resistance. Elevated FFA levels cause a reduction in insulin-stimulated IRS-1 phosphorylation, IRS-1-associated PI 3-K activity, and increased hepatic glucose production via gluconeogenesis. Higher levels of FFA shift substrate preference from glucose to FFA in the muscle tissue oxidation, further contributing to hyperglycemia. Long-term exposure of pancreatic β-cells to FFA diminishes their insulin secretory response to glucose. Adipose tissue also secretes a variety of hormones



(adipokines) that regulate various cellular processes, including energy expenditure. A higher expression of TNF-α in adipose tissue of obese subjects has been linked to insulin resistance. TNF-α is known to impair insulin signaling through IRS-1 serine phosphorylation and through reduced expression of IRS-1 and GLUT4. Deficiency of leptin, another hormone of adipose origin, is also linked with insulin resistance in db/db and ob/ob mice. Leptin replacement improves glycemic control and reduces circulating lipid levels. Resistin, another hormone of adipose origin, is found at much higher levels in animal models of diabetes and obesity, and treatments with insulin sensitizing agents, such as thiazolidinediones (TZD) reduces circulating levels of resistin. TZDs also reduce the expression of adiponectin, an insulin-sensitizing factor in adipose tissue, which reduces serum FFAs by promoting their flux into adipose tissue.

TZDs belong to a new class of insulin sensitizers that are used for the treatment of type II diabetes. They act as direct, high-affinity ligands of peroxisome proliferator-activated receptor γ (PPARγ), an adipocyte-specific nuclear hormone receptor. Although PPARγ is expressed in most organs, the level of PPARγ mRNA is about 50-fold higher in adipose tissue. When compared to some natural ligands, such as 15-deoxy-Δ 12, 14-prostaglandin J2, TZDs exhibit much higher affinity for PPARγ (EC_{50} = 20-400 nM). In the cell, PPARγ forms a heterodimer with the retinoid X receptor (RXR). Without TZD binding the heterodimer is associated with a co-repressor complex that includes a histone deacetylase, which keeps DNA in a transcriptionally repressed state. Upon TZD binding to PPARγ, the co-repressor complex dissociates and a co-activator complex containing histone acetylase associates. This promotes binding of the PPARγ-RXR complex to PPAR response elements (PPRE) in target genes resulting in modification of the transcription of these genes. PPREs are commonly found in genes involved in lipid metabolism and energy balance, including those encoding lipoprotein lipase, adipocyte fatty acid binding protein, fatty acyl-CoA synthase, glucokinase, and the glucose transporter GLUT4.

TZDs may also have cardiovascular benefits in type II diabetic subjects who exhibit metabolic syndrome X, which is characterized by clustering of atherosclerotic cardiovascular disease risk factors, including insulin resistance, obesity, hypertension, and hyperlipidemia. The characteristic features of metabolic syndrome X emerge from interactions between molecular pathways of glucose and lipid metabolism and blood pressure control. Insulin is known to promote the activity of lipoprotein lipase, which participates in converting VLDL into LDL. A few clinical studies have shown that TZDs raise HDL levels, reduce triglyceride levels, and improve endothelium-mediated vasodilatation. TZD-induced activation of PPARγ triggers signaling from adipocytes to skeletal muscle, which ameliorates insulin resistance. This may be linked to a significant reduction of FFA levels by TZDs.

It is widely recognized that cardiovascular complications observed in type II diabetes develop through inflammatory and procoagulant pathways with increased oxidative stress. In addition to their insulin-sensitizing effects, TZDs also exhibit antioxidant, anti-inflammatory, and anti-procoagulant properties. These important links have increased our understanding of the relationship between hyperglycemia, insulin resistance, obesity, and the onset of cardiovascular disease.

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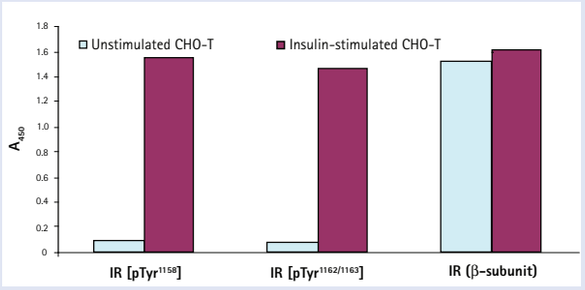
Insulin Receptor Assay Kits

Insulin Receptor (β-subunit) ELISA Kit

Format: 96-well plate. Sensitivity: < 0.5 ng/ml.
Assay time: 4 h. Sample type: Cells
Suitable for detection and quantitation of insulin receptor (IR) β-subunit, independent of its phosphorylation status. Although this kit is designed for use with human cell lines, it cross-reacts with mouse and rat cells.

Cat. No. CBA039 **1 kit** **€ 704**



CHO-T cells were stimulated for 10 minutes with 100 nM insulin. Unstimulated cells were used as control. This kit (Cat. No. CBA039) detects phosphorylated IR in stimulated CHO-T cells and non-phosphorylated IR in control cells.

PhosphoDetect™ Insulin Receptor (pTyr$^{1162/1163}$) ELISA Kit

Format: 96-well plate. Sensitivity: < 0.8 unit/ml. Assay time: 4 h. Sample type: Cells
Suitable for detection and quantitation of insulin receptor (IR) phosphorylated at Tyr$^{1162/1163}$. Although this kit is designed for use with human cell lines, platelets, and lymphocytes, it cross-reacts with mouse and rat cells.

Cat. No. CBA038 **1 kit** **€ 704**

Antibodies for Diabetes Related Research

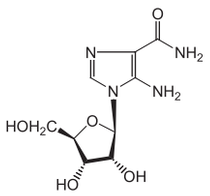
Name	Cat. No.	Comments	Size	Price
Anti-PAN TORC (1-42) Rabbit pAb	ST1098	Recognizes the ~79 kDa TORC1, TORC2, and TORC3 proteins in 293T cells over-expressing TORC1, TORC2, or TORC3. Reacts with human, mouse, rat. **IB, IP**	50 µl	€ 122
Anti-TORC2 (454-607) Rabbit pAb	ST1099	Recognizes the ~79-85 kDa TORC2 protein in primary hepatocytes. Reacts with human, mouse, rat. **IB, IP**	50 µl	€ 122
PhosphoDetect™ Anti-IR/IGF1R (pTyr$^{1158/1162/1163}$) Rabbit pAb	PS1009	Recognizes the ~100 kDa IR/IGF1R protein phosphorylated at Tyr$^{1158/1162/1163}$. Reacts with human, mouse. **IB**	100 µl	€ 295
PhosphoDetect™ Anti-IRS1 (pTyr^{612}) Rabbit pAb	PS1010	Recognizes the ~165-180 kDa IRS-1 protein phosphorylated at Tyr^{612}. Reacts with human. **IB**	10 T	€ 295
Anti-Leptin Receptor Rabbit pAb	431005	Recognizes the ~150 kDa leptin receptor protein. Reacts with mouse, rat. **ELISA, IB**	50 µg	€ 324
Anti-Leptin Rabbit pAb	431003	Recognizes the ~16 kDa leptin protein. Reacts with mouse, rat. **ELISA, IB, RIA**	100 µl	€ 332
PhosphoDetect™ Anti-Leptin Receptor (pTyr^{985}) Rabbit pAb	431006	Recognizes the ~150 kDa leptin receptor protein phosphorylated at Tyr^{985}. Reacts with human, mouse. **IB, IP**	50 µg	€ 259

ELISA: enzyme-linked immunosorbent assay; **IB**: immunoblotting; **IP**: immunoprecipitation; **RIA**: radioimmunoassay; **10 T**: 10 tests by Western miniblot

Activators and Inhibitors for Diabetes Related Research

AICA-Riboside

A cell-permeable nucleoside compound whose phosphorylated metabolite activates adenosine monophosphate-activated protein kinase (AMPK) and acts as a regulator of *de novo* purine synthesis. Stimulates glucose uptake in perfused and isolated muscle. *Purity: ≥98% by HPLC.* M.W. 258.2



Cat. No. 123040 **50 mg** **€ 100**

Ref.: Culmsee, C., et al. 2001. *J. Mol. Neurosci.* **17,** 45; Muoio, D.M., et al. 1999. *Biochem. J.* **338,** 783; Hayashi, T., et al. 1998. *Diabetes* **47,** 1369; Corton, J.M., et al. 1995. *Eur. J. Biochem.* **229,** 558.

AICA-Riboside, 5′-Phosphate

A 5′-phosphorylated analog of AICA-Riboside (Cat. No. 123040) that mimics AMP and acts as an activator of AMPK (AMP-activated protein kinase). *Purity: ≥95% by HPLC.* M.W. 338.2

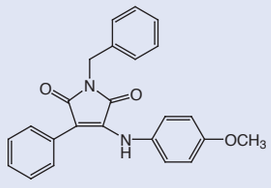
Cat. No. 123041 **25 mg** **€ 171**

Ref.: Fryer, L.G.D., et al. 2002. *Biochem. J.* **363,** 167; Henin, N., et al. 1996. *Biochim. Biophys. Acta* **1290,** 197; Corton, J.M., et al. 1995. *Eur. J. Biochem.* **229,** 558; Sullivan, J.E., et al. 1994. *Biochem. Biophys. Res. Commun.* **200,** 1551.

LXRα/β Agonist

[3-((4-Methoxyphenyl)amino)-4-phenyl-1-(phenylmethyl)-1H-pyrrole-2,5-dione]

A cell-permeable, potent agonist of liver X receptor (EC_{50} = 50 nM and 40 nM for LXRα-SRC1 and LXRβ-SRC1, respectively). Displays ~50-fold greater selectivity for LXR over a panel of nuclear receptors, including FXR, PPARα/γ/δ, PXR, AR, ERα/β, GR, and PR. *Purity: ≥98% by HPLC.* M.W. 384.4



Cat. No. 440165 **10 mg** **€ 122**

Ref.: Jaye, M.C., et al. 2005. *J. Med. Chem.* **48,** 5419.

AMPK Activator

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

A cell-permeable, indirect activator of AMPK (AMP-activated Protein Kinase) that targets mitochondrial complex I. Causes an elevation in cellular AMP levels and is shown to enhance glucose uptake in L6 myocytes (EC_{50} = 11.7 µM), and reduce blood glucose levels in ZDF rats. *Purity: ≥95% by HPLC.* M.W. 368.4

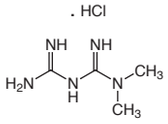
Cat. No. 171256 **5 mg** **€ 122**

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

1,1-Dimethylbiguanide, Hydrochloride

(Metformin)

An antihyperglycemic agent that lowers blood glucose levels without stimulating insulin secretion. Reported to stimulate AMP-activated protein kinase (AMPK) leading to the reduction in acetyl-CoA carboxylase activity and induction of fatty acid oxidation. *Purity: ≥98% by TLC.* M.W. 165.6

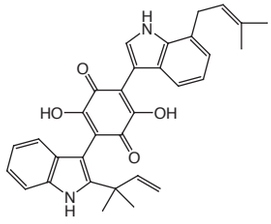


Cat. No. 317240 **5 g** **€ 62**

Ref.: Cleasby, M.E., et al. 2004. *Diabetes* **53,** 3258; Klein, J., et al. 2004. *J. Endocrinol.* **183,** 299; Zhou, G., et al. 2001. *J. Clin. Invest.* **108,** 1167; Lin, H.Z., et al. 2000. *Nat. Med.* **6,** 998.

Demethylasterriquinone B1

A cell-permeable, insulin mimic with oral anti-diabetic activity. Selectively stimulates insulin receptor (IR) tyrosine kinase activity (EC_{50} ~ 6 µM in CHO•IR cells) with little effect towards IGF-1R, EGFR, or PDGFR. *Purity: ≥97% by HPLC.*M.W. 506.6



Cat. No. 260010 **5 mg** **€ 249**

Ref.: Webster, N.J., et al. 2003. *Chembiochem* **4,** 379; Pirrung, M.C., et al. 2002. *J. Org. Chem.* **6,** 23; Westerlund, J., et al. 2002. *Diabetes* **51,** S50; Roper, M.G., et al. 2002. *Diabetes* **51,** S43; Liu, K., et al. 2000. *J. Med. Chem.* **43,** 3487; Zhang, B., et al. 1999. *Science* **284,** 974.

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Activators and Inhibitors for Diabetes Related Research *continued...*

IGF-1R Inhibitor, PPP

(Insulin-like Growth Factor-1 Receptor Inhibitor; Picropodophyllin)

A cell-permeable, non-competitive, potent, and specific inhibitor of IGF-1R both *in vitro* (IC_{50} = 1 nM in cell-free kinase assay; ≤ 60 nM for cell viability and receptor autophosphorylation in melanoma cell lines) and *in vivo*. Exhibits little effect towards IR, FGFR, PDGFR and EGFR. Targets the phosphorylation of Tyr^{1136} in the activation loop and is the first inhibitor reported to discriminate between IGF-1R and IR. *Purity: ≥95% by HPLC.* M.W. 414.4

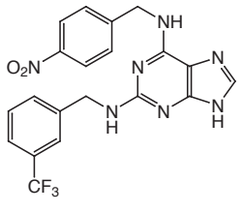
Cat. No. 407247 **1 mg** **€ 112**

Ref.: Mazitschek, R., and Giannis, A. 2004. *Curr. Opin. Chem. Biol.* **8,** 432; Vasilcanu, D., et al. 2004. *Oncogene* **23,** 7854; Girnita, A., et al. 2004. *Cancer Res.* **64,** 236.

IP3K Inhibitor

[Inositol-1,4,5-trisphosphate 3-Kinase Inhibitor; N^2-(*m*-Trifluorobenzyl), N^6-(*p*-nitrobenzyl)purine]

A cell-permeable, selective, ATP-competitive inhibitor of IP 3-K (IC_{50} = 10.2 µM). Increases cellular IP3 levels and Ca^{2+}-release in a dose-dependent manner (5 to 20 µM in HL60 cells). *Purity: ≥95% by HPLC.* M.W. 443.4



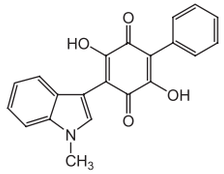
Cat. No. 406170 **5 mg** **€ 104**

Ref.: Chang, Y.T., et al. 2002. *ChemBioChem* **3,** 897.

IRTK Activator

[2,5-Dihydroxy-3-(1-methylindol-3-yl)-6-phenyl-1,4-benzoquinone]

A potent and highly selective activator of insulin receptor tyrosine kinase (IRTK; EC_{50} = 300 nM in CHO cells expressing human insulin receptor). Does not activate other closely related receptors such as IGF-IR, EGFR, and PDGFR at concentrations up to 30 µM. *Purity: ≥97% by HPLC.* M.W. 345.4



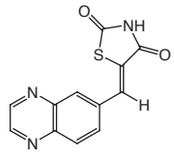
Cat. No. 420295 **5 mg** **€ 102**

Ref.: Liu, K., et al. 2000. *J. Med. Chem.* **43,** 3487; Qureshi, S.A., et al. 2000. *J. Biol. Chem.* **275,** 36590.

PI 3-Kγ Inhibitor

(5-Quinoxalin-6-ylmethylene-thiazolidine-2,4-dione)

A cell-permeable thiazolidinedione compound that acts as a potent, selective, and ATP-competitive inhibitor of PI 3-Kγ (IC_{50} = 8 nM, 60 nM, 270 nM, 300 nM for p110-γ, α, β and δ-isoforms, respectively). *Purity: ≥90% by HPLC.* M.W. 257.3



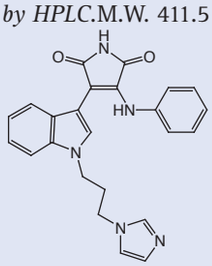
Cat. No. 528106 **5 mg** **€ 122**

Ref.: Barber, D.F., et al. 2005. *Nat. Med.* **11,** 933; Camps, M., et al. 2005. *Nat. Med.* **11,** 936.

PKC_{β} Inhibitor

[3-(1-(3-Imidazol-1-ylpropyl)-1H-indol-3-yl)-4-anilino-1H-pyrrole-2,5-dione]

A potent and ATP-competitive inhibitor of PKC_{β} (IC_{50} = 5 nM and 21 nM for human $PKC_{\beta II}$ and $_{\beta I}$, respectively). *Purity: ≥90% by HPLC.*M.W. 411.5



Cat. No. 539654 **500 µg** **€ 150**

Ref.: Tanaka, M., et al. 2004. *Bioorg. Med. Chem. Lett.* **14,** 5171.

T0901317

{N-(2,2,2-Trifluoroethyl)-N-[4-(2,2,2-trifluoro-1-hydroxy-1-trifluoromethylethyl)phenyl]sulfonamide}

A cell-permeable, nonsterol, benzenesulfonamide compound that acts as a highly selective and potent liver X receptor agonist (EC_{50} = 20 nM for LXR_{α}). Induces expression of genes associated with fatty acid biosynthesis and raises levels of serum HDL cholesterol. Shown to lower plasma glucose in diabetic rodents. *Purity: ≥98% by TLC.*M.W. 481.3

Cat. No. 575310 **10 mg** **€ 121**

Ref.: Fukumoto, H., et al. 2003. *J. Biol. Chem.* **277,** 48508; Terasaka, N., et al. 2003. *FEBS Lett.* **536,** 6; Cao, G., et al. 2002. *J. Biol. Chem.* **278,** 1131; DeBose-Boyd, R.A., et al. 2001. *Proc. Natl. Acad. Sci. USA* **98,** 1477; Schultz, J.R., et al. 2000. *Genes Dev.* **14,** 2831.

NEW Glucagon Receptor Antagonists

Glucagon Receptor Antagonist I

[N-(3-Cyano-6-(1,1-dimethylpropyl)-4,5,6,7-tetrahydro-1-benzothien-2-yl)-2-ethylbutanamide]

A cell-permeable, potent, selective, and competitive antagonist of the glucagon receptor. Binds to hGCGR with high affinity and prevents its interaction with glucagon (IC_{50} = 181 nM, K_{DB} = 81 nM, and *p*A2 = 7.1 in membranes prepared from CHO-hGCGR). Also suppresses glucagon-induced glycogenolysis in primary hepatocytes. *Purity: ≥95% by HPLC.* M.W. 346.5

Cat. No. 346001	**1 mg**	**€ 104**
	5 mg	**€ 324**

Ref.: Qureshi, S.A., et al. 2004. *Diabetes* **53,** 3267.

Glucagon Receptor Antagonist, Control

[N-(3-Cyano-6-(1,1-dimethylpropyl)-4,5,6,7-tetrahydro-1-benzothien-2-yl)-4-bromobenzamide]

A cell-permeable inactive control for Glucagon Receptor Antagonist (Cat. No. 346001). Displays weak affinity to hGCGR. *Purity: ≥95% by HPLC.* M.W. 431.4

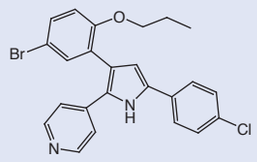
Cat. No. 346002	**1 mg**	**€ 104**
	5 mg	**€ 324**

Ref.: Qureshi, S.A., et al. 2004. *Diabetes* **53,** 3267.

Glucagon Receptor Antagonist II

[L-168,049; 2-(4-Pyridyl)-5-(4-chlorophenyl)-3-(5-bromo-2-propyloxyphenyl)pyrrole]

A cell-permeable, selective, non-competitive, high affinity glucagon receptor antagonist (IC_{50} = 3.7 nM, 63 nM, and 60 nM for inhibition of labeled glucagon binding to human, murine, and canine glucagon receptor, respectively). Exhibits diminished antagonistic properties in the presence of Mg^{2+}. *Purity: ≥98% by HPLC.* M.W. 467.8



Cat. No. 346003	**5 mg**	**€ 104**

Ref.: Dallas-Yang, Q., et al. 2002. *Anal. Biochem.* **301,** 156; Cascieri, M.A., et al. 1999. *J. Biol. Chem.* **274,** 8694; de Laszlo, S.E., et al. 1999. *Bioorg. Med. Chem. Lett.* **9,** 641.

Interested in Obesity-Related Research?

Leptin, Human, Recombinant, *E. coli*

(rhOB)

A product of the obese (*ob*) gene that serves as a ligand for the OB receptor. Mice with mutations of the *ob* gene have been found to be obese and diabetic. Reduces hepatic glucose production by blocking phosphoenolpyruvate synthesis. *Purity: ≥97% by SDS-PAGE.* M.W. 16,000

Cat. No. 429700	**1 mg**	**€ 256**
	5 mg	**€ 698**

Ref.: *Merck Index* **13,** 5462; Anderwald, C., et al. 2002. *Mol. Endocrinol.* **16,** 1612; Ookuma, M., et al. 1998. *Diabetes* **47,** 219; Campfield, L.A., et al. 1995. *Science* **269,** 546; Halaas, J.L., et al. 1995. *Science* **269,** 543; Pelleymounter, M.A., et al. 1995. *Science* **269,** 540; Zhang, Y., et al. 1994. *Nature* **372,** 425.

Also available...

Leptin, Mouse, Recombinant, *E. coli*

(βrmOB)

*Purity: ≥97% by SDS-PAGE.*M.W. 16,000

Cat. No. 429705	**1 mg**	**€ 256**
	5 mg	**€ 698**

NEW Obestatin, Human, Synthetic

(H-FNAPFDVGIKLSGVQYQQHSQAL-NH_2)

A ghrelin-associated 23-mer peptide that acts as an anorexic hormone. Shown to activate the orphan G protein-coupled receptor GPR39 (K_d = 1 nM) and stimulate cAMP production in GPR39-CHO and GPR39-HEK293T cells. Suppresses cumulative food intake, inhibits jejunal contraction and decreases body weight gain in mice. *Purity: ≥97% by HPLC.* M.W. 2546.9

Cat. No. 494125	**2 mg**	**€ 140**

Ref.: Zhang, J.V., et al. 2005. *Science* **310,** 996.

Peroxisome Proliferator-Activated Receptors: New Therapeutic Targets in Diabetes

Peroxisome proliferator-activated receptors (PPARs) are members of the nuclear hormone receptor family of transcription factors that mediate a variety of cellular processes, including glucose and lipid metabolism, inflammatory responses, and regulation of apoptotic cell death. They act by binding to specific peroxisome proliferator-response elements (PPREs) on target genes. Three forms of PPARs have been described, which are designated as α, δ, and γ forms. They contain a DNA binding domain and a ligand-binding domain. Each form is expressed in different tissues and can be activated by different ligands, most of them being specific for one form of PPAR. PPARα is expressed in skeletal muscle, liver, kidney, and endothelial cells and regulates lipoprotein metabolism. Its transcriptional activity is enhanced in the presence of insulin. PPARδ is shown to be widely distributed in animal tissues and is reported to be involved in oligodendrocyte differentiation. It is expressed to higher levels in brain, adipose tissue, and skin. PPARγ is the most studied isoform and plays a critical role in adipocyte differentiation and fat deposition.

PPARγ is shown to mediate the antidiabetic and adipogenic actions of the thiazolidinediones (TZD), a new class of insulin sensitizers, which are under clinical trials for the treatment of Type II diabetes. TZDs are highly selective, high-affinity ligands of PPARγ with minimal activity towards the α and β forms. Although PPARγ is expressed in most organs, the level of PPARγ mRNA is about 50-fold higher in the adipose tissue.

Purified Peroxisome Proliferator-Activated Receptors

PPARα, Human, Recombinant, *E. coli*

(Peroxisome Proliferator-Activated Receptor, α-isotype)

Expressed in *E. coli* with an N-terminal His•Tag® sequence. Useful for gel mobility and protein-protein interaction assays. PPARα is highly expressed in brown adipose tissue and liver, and to some extent in the kidney, heart, and skeletal muscle. The target genes of PPARα are a relatively homogeneous group of genes that participate in various aspects of lipid metabolism such as fatty acid uptake through membranes, fatty acid binding in cells, fatty acid oxidation, and lipoprotein assembly and transport. *Purity: ≥95% by SDS-PAGE.* M.W. 52,000. Note: 1 unit = 1 ng protein.

Cat. No. 516559 **10 KU** **€ 405**

Ref.: Kersten, S. 2001. *EMBO Rep.* **21,** 282; Kersten, S., et al. 2000. *Nature* **405,** 421; Willson, T.M., et al. 2000. *J. Med. Chem.* **43,** 527; Desvergne, B., and Wahli, W. 1999. *Endocr. Rev.* **20,** 649.

PPARδ, Human, Recombinant, *E. coli*

(Peroxisome Proliferator-Activated Receptor, δ-isotype)

Expressed in *E. coli* with an N-terminal His•Tag® sequence. Useful for gel mobility and protein-protein interaction assays. PPARδ displays a high level of expression in lipid-metabolizing tissues such as adipose tissue, small intestine, heart, and skeletal muscle, and it can regulate the expression of genes implicated in fatty acid uptake and activation. It has been implicated in fatty acid-induced proliferation in 3T3C2 cells and been shown to participate in embryo implantation and decidualization. *Purity: ≥95% by SDS-PAGE.* M.W. 49,000. Note: 1 unit = 1 ng protein.

Cat. No. 516564 **10 KU** **€ 405**

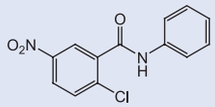
Ref.: Bastie, C. 2002. *Bull. Cancer* **89,** 23; Kersten, S. 2001. *EMBO Rep.* **21,** 282; Bastie, C., et al. 2000. *J. Biol. Chem.* **275,** 38768; Jehl-Petrie, C., et al. 2000. *Biochem. J.* **350 Pt 1,** 93; Kersten, S., et al. 2000. *Nature* **405,** 421; Willson, T.M., et al. 2000. *J. Med. Chem.* **43,** 527; Lim, H., et al. 1999. *Genes Dev.* **13,** 1561.

PPAR Antagonists

GW9662

(2-Chloro-5-nitro-N-phenylbenzamide)

A cell-permeable, selective, and irreversible PPARγ antagonist (IC_{50} = 3.3 nM, 32 nM, and 2 µM for PPARγ, PPARα, and PPARδ, respectively). Reported to covalently modify a cysteine residue in the binding site of PPAR. *Purity: ≥95% by HPLC.* M.W. 276.7



Cat. No. 370700 **5 mg** **€ 64**

Ref.: Leesnitzer, L.M., et al. 2002. *Biochemistry* **41,** 6640; Willson, T.M., et al. 2000. *J. Med. Chem.* **43,** 527; Huang, J.T., et al. 1999. *Nature* **400,** 378.

T0070907

[2-Chloro-5-nitro-N-(4-pyridyl)benzamide]

A cell-permeable, potent, specific, irreversible, and high-affinity antagonist of PPARγ (K_i = 1 nM). Displays >800-fold greater selectivity for PPARγ over PPARα and PPARδ (K_i = 850 nM and 1.8 µM, respectively). Suppresses interactions between PPARγ and coactivator-derived peptides and promotes the recruitment of corepressor-derived peptides. *Purity: ≥97% by HPLC.* M.W. 277.7

Cat. No. 575305 **5 mg** **€ 112**

Ref.: Lee, G., et al. 2002. *J. Biol. Chem.* **277,** 19649.

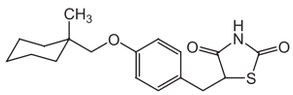
Learn more about PPARs and diabetes: www.calbiochem.com/PPAR

PPAR Agonists

Ciglitazone

{(±)-5-[4-(1-Methylcyclohexylmethoxy)benzyl]thiazolidine-2,4-dione}

A potent thiazolinedione type anti-hyperglycemic agent and a selective PPARγ agonist (EC_{50} = 3 µM). *Purity: ≥98% by TLC.* M.W. 333.5



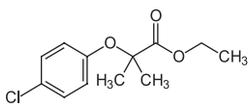
Cat. No. 230950 **5 mg** **€ 128**

Ref.: Jha, R.J. 1999. *Clin. Exp. Hypertens.* **21,** 157; Xin, X., et al. 1999. *J. Biol. Chem.* **274,** 9116; Lohrke, B., et al. 1998. *J. Endocrinol.* **159,** 429; Cantello, B.C., et al. 1994. *J. Med. Chem.* **37,** 3977.

Clofibrate

[2-(4-Chlorophenoxy)-2-methylpropanoic Acid Ethyl Ester]

An anti-hyperlipoproteinemic agent that acts by inhibiting cholesterol biosynthesis. Activates PPARα and induces cytochrome P450 4A1 and 4A3. *Purity: ≥98% by TLC.* M.W. 242.7

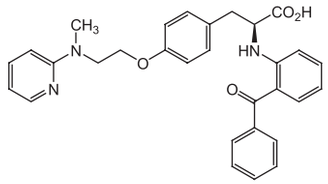


Cat. No. 231405 **500 mg** **€ 45**

Ref.: Manautou, J.E., et al. 1996. *Toxicol. Appl. Pharmacol.* **140,** 30; Brass, E.P., and Ruff, L.J. 1991. *J. Pharmacol. Exp. Ther.* **257,** 1034; Aoyama, T., et al. 1990. *J. Lipid. Res.* **31,** 1477.

GW1929

A potent, tyrosine-based PPARγ agonist (EC_{50} = 13 nM for murine receptor and 6.2 nM for human receptor in cell-based transactivation assays). *Purity: ≥95% by HPLC.* M.W. 495.6



Cat. No. 370695 **1 mg** **€ 299**

Ref.: Han, S., et al. 2004. *Clin. Cancer Res.* **10,** 1911; Willson, T.M., et al. 2000. *J. Med. Chem.* **43,** 527; Brown, K.K., et al. 1999. *Diabetes* **48,** 1415.

GW7647

[2-(4-(2-(1-Cyclohexanebutyl-3-cyclohexylureido)ethyl)phenylthio)-2-methylpropionic Acid; GW647]

A cell-permeable, potent, and selective PPARα agonist (PPARα, γ, and δ - EC_{50} = 6 nM, 1.1 µM, and 6.2 µM for human; 1 nM, 1.3 µM, and 2.9 µM for murine, respectively). Also displays *in vivo* lipid-lowering activity in rats. *Purity: ≥98% by HPLC.* M.W. 502.8

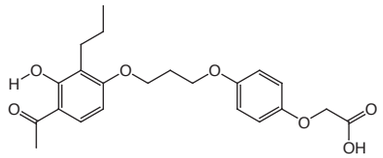
Cat. No. 370698 **5 mg** **€ 191**

Ref.: Muoio, D.M., et al. 2002. *J. Biol. Chem.* **277,** 26089; Oliver, W.R. Jr., et al. 2001. *Proc. Natl. Acad. Sci. USA* **98,** 5306; Poirier, H., et al. 2001. *Biochem. J.* **355,** 481.

PPAR Agonists *continued...*

L-165,041
{4-[3-(2-Propyl-3-hydroxy-4-acetyl)phenoxy]propyloxyphenoxy-acetic acid; Compound P; L165041}

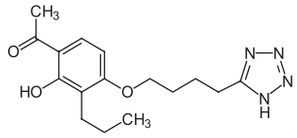
A cell-permeable, potent, and selective PPARδ agonist (K_i = 6 nM for hPPARδ and 730 nM for hPPARγ). Induces adipocyte differentiation in NIH-PPARδ cells at 500 nM. Inhibits cytokine-induced expression of VCAM-1 (vascular cell adhesion molecule-1) and the secretion of MCP-1 (monocyte chemotactic protein-1) in EAhy926 cells. *Purity: ≥98% by HPLC.* M.W. 402.4



Cat. No. 422175 **5 mg** **€ 118**

Ref.: Rival, Y., et al. 2002. *Eur. J. Pharmacol.* **435,** 143; Son, C., et al. 2001. *Endocrinology* **142,** 4189; Castrillo, A., et al. 2001. *J. Biol. Chem.* **276,** 34082; Hansen, J.B., et al. 2001. *J. Biol. Chem.* **276,** 3175; Leibowitz, M.D., et al. 2000. *FEBS Lett.* **473,** 333; Berger, J., et al. 1999. *J. Biol. Chem.* **274,** 6718; Lim, H., et al. 1999. *Genes Dev.* **13,** 1561.

LY 171883
A selective, orally active leukotriene D_4 antagonist (K_i = 630 nM for ^{3}H-LTD$_4$ binding to guinea pig lung membranes). A relatively weak agonist of PPARs. *Purity: ≥98% by TLC.* M.W. 318.4



Cat. No. 440198 **10 mg** **€ 75**

Ref.: Yu, C., et al. 2004. *Eur. J. Biochem.* **271,** 386; Cannon, J.R., and Eacho, P.I. 1991. *Biochem. J.* **280,** 387; Aharony, D., et al. 1987. *J. Pharmacol. Exp. Ther.* **243,** 921; Fleisch, J.H., et al. 1985. *J. Pharmacol. Exp. Ther.* **233,** 148.

PPAR$_\gamma$ Activator, Fmoc-Leu
(F-L-Leu)

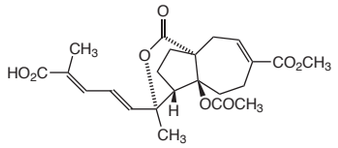
An N-protected leucine analog that acts as a selective modulator of PPARγ (K_i = 15 µM). Displays weaker adipogenic activity than other nuclear receptor ligands. Two molecules of F-L-Leu interact with one PPARγ molecule in a highly specific manner. Exhibits potent insulin sensitizing activity. *Purity: ≥99% by HPLC.* M.W. 353.4

Cat. No. 344034 **250 mg** **€ 43**

Ref.: Rocchi, S., et al. 2001. *Mol. Cell* **8,** 737.

Pseudolaric Acid B, *Pseudolarix kaempferi*
(PLAB)

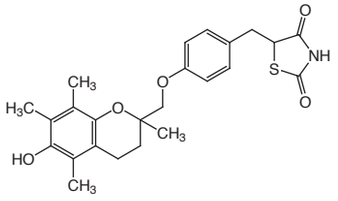
A cell-permeable triterpenoid lactone with potent antifungal, antimicrobial, antifertility, and cytotoxic properties. Shown to activate PPARα, γ, and δ-isoforms equipotently (EC_{50} ~ 100 µM) in CV-1 and H4IIEC3 mammalian cell lines. *Purity: ≥95% by NMR.* M.W. 432.5



Cat. No. 539595 **1 mg** **€ 209**

Ref.: Jardat, M.S., et al. 2002. *Planta Med.* **68,** 667; Li, E., et al. 1995. *J. Nat. Prod.* **58,** 57.

Troglitazone
An α-tocopherol moiety containing thiazolidinedione class of insulin-sensitizer that acts as an activator of PPARγ. Exhibits anti-proliferative and anti-inflammatory properties. Exerts positive inotropic effect via Ca^{2+} sensitization in the sarcoplasmic reticulum and inhibits Na^+/H^+ exchange activity and proliferation of macrovascular endothelial cells. *Purity: ≥98% by TLC.* M.W. 441.5



Cat. No. 648469 **5 mg** **€ 141**

Ref.: Furuse, Y., et al. 2001. *Br. J. Pharmacol.* **133,** 1307; Ghanim, H., et al. 2001. *J. Clin. Endocrinol. Metab.* **86,** 1306; Goetze, S., et al. 2001. *J. Cardiovasc. Pharmacol.* **38,** 909; Rosen, E.D., and Spiegelman, B.M., 2001. *J. Biol. Chem.* **276,** 37731; Subbaramaiah, K., et al. 2001. *J. Biol. Chem.* **276,** 12440; Takeda, K., et al. 2001. *J. Biol. Chem.* **276,** 48950; Tanaka, T., et al. 2001. *Cancer Res.* **61,** 2424; Wakino, S., et al. 2001. *J. Biol. Chem.* **276,** 47650.

WY-14643
{[4-Chloro-6-(2,3-xylidino)-2-pyrimidinylthio]acetic Acid}

A potent PPARα ligand. Inhibits TNF-α induced expression of VCAM-1 in endothelial cells. *Purity: ≥98% by TLC.* M.W. 323.8

Cat. No. 681725 **50 mg** **€ 94**

Ref.: Marx, N., et al. 1999. *Circulation* **99,** 3125; Murakami, K., et al. 1999. *Biochem. Biophys. Res. Commun.* **260,** 609; Keller, H., et al. 1993. *Proc. Natl. Acad. Sci. USA* **90,** 2160; Keller, H., and Wahli, W. 1993. *Trends Endocrinol. Metab.* **4,** 291; Dreyer, C., et al. 1992. *Cell* **68,** 879; Issemann, I., and Green, S. 1990. *Nature* **347,** 645.

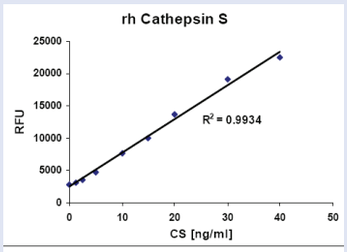
NEW Protease Assay Kits and Protease Inhibitors

InnoZyme™ Cathepsin S Activity Assay Kit

Assay range: 1–40 ng/ml

A specific and sensitive assay kit for measuring active human Cathepsin S in cell lysates and tissue extracts and to screen Cathepsin S inhibitors. Assay uses a monoclonal antibody specific for human Cathepsin S immobilized on a 96-well plate. Activity of the captured Cathepsin S is measured using Z-Val-Val-Arg-AMC substrate.

Cat. No. CBA050 **1 kit** **€ 383**



Activity of human recombinant Cathepsin S measured using InnoZyme™ Cathepsin S Activity Assay Kit (Cat. No. CBA050).

InnoZyme™ TACE Activity Kit

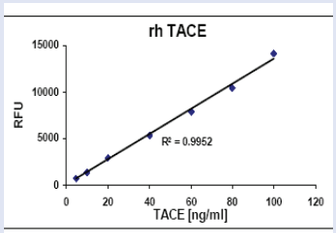
(α-Secretase Activity Kit; ADAM17 Activity Kit; TNF-α Converting Enzyme Activity Kit)

Assay range: 5–100 ng/ml

The InnoZyme™ TACE Activity Kit is a specific and sensitive assay designed to measure human TACE activity in cell lysates and biological samples, and for screening enzyme inhibitors. Assay utilizes an Anti-Human TACE-coated 96-well plate pre-coated with a monoclonal antibody specific for human TACE that captures the enzyme. Activity of captured TACE is measured using an internally quenched fluorescent substrate, MCA-KPLGL-Dpa-AR-NH_2. Cleavage of the scissile amide bond, G-L, releases the fluorophore from the quenching molecule, Dpa, resulting in an increase in fluorescence.

(Ex. max. = ~324 nm, Em. max. = ~400 nm)

Cat. No. CBA042 **1 kit** **€ 520**



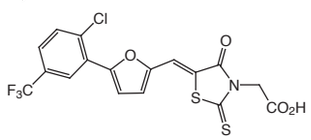
Activity of recombinant TACE (Cat. No. PF133) measured using InnoZyme™ TACE Activity Kit (Cat. No. CBA042).

Anthrax Lethal Factor Protease Inhibitor III

[5-(5-(2-Chloro-5-trifluoromethyl-phenyl)-furan-2-ylmethylene)-4-oxo-2-thioxo-thiazolidin-3-yl)-acetic acid]

A cell-permeable, rhodanine-acetic acid analog that chelates the active site Zn^{2+} and inhibits anthrax lethal factor (LF) metalloproteinase (K_i = 32 nM). Has only a minimal inhibitory effect on MMP-2 and MMP-9. Shown to effectively prevent LF-induced MAPKK1 proteolysis (< 2 µM) and offer protection against LF and protective antigen cytotoxic effects in RAW264.7 cells (IC_{50} < 5 µM). In combination with ciprofloxacin doubly enhances the survival rates of mice challenged with anthrax spores.

Purity: ≥*95% by HPLC.*M.W. 447.8

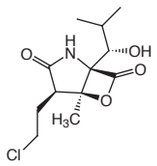


Cat. No. 176910 **5 mg** **€ 113**

Ref.: Forino, M., et al. 2005. *Proc. Natl. Acad. Sci. USA* **102,** 9499.

Proteasome Inhibitor VII, Antiprotealide

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



Cat. No. 539179 **50 µg** **€ 158**

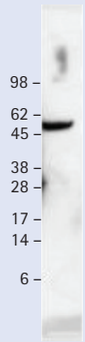
Ref.: Reddy, L.R., et al. 2005. *J. Am. Chem. Soc.* **127,** 8974.

www.calbiochem.com/inhibitors/protease

Interested in Matrix-Metalloproteinase Research?

Anti-MMP-12 (Ab-2) Rabbit pAb

Immunogen used was a recombinant human MMP-12 containing an N-terminal His•Tag® sequence. Recognizes the ~54 kDa latent form of the MMP-12 protein. May also detect the ~45 kDa active form of MMP-12.



Detection of human MMP-12. Sample: concentrated serum-free culture medium from human cells. Primary antibody: Anti-MMP-12 Rabbit pAb (Ab-2) (Cat. No. IM1013) (1:1000). Detection: chemiluminescence.

Cat. No. IM1013 **50 µl** **€ 159**

Ref.: Impola, U., et al. 2004. *J. Pathol* **202,** 14; Kerkela, E., et al. 2002. *J. Pathol* **198,** 258; Kerkela, E., et al. 2001. *Bone* **29,** 487; Raza, S.L., et al. 2000. *J. Biol. Chem.* **275,** 41243;

Active MMP-13 ELISA Kit

Sensitivity: 7 pg/ml
Assay range: 32–200 pg/ml
A highly sensitive and specific kit for detection of active MMP-13 from human serum, synovial fluid, and cell culture supernatant. Does not recognize MMP-1, MMP-2, MMP-3, MMP-8, MMP-9, or the latent form of MMP-13.

Cat. No. QIA130 **1 kit** **€ 654**

NEW MMP-13, Human, Recombinant, Active

An APMA-free, active form of MMP-13. Specific activity: ≥50 mU/mg protein. M.W. 52,000

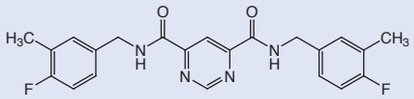
Cat. No. 444287 **5 µg** **€ 221**

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

MMP-13 Inhibitor

[Pyrimidine-4,6-dicarboxylic acid, *bis*-(4-fluoro-3-methyl-benzylamide)]

A pyrimidine dicarboxamide compound that potently inhibits MMP-13 activity (IC_{50} = 8 nM). Shown to bind to the MMP-13 catalytic domain and act as a non-zinc-chelating inhibitor. *Purity: ≥98% by HPLC.* M.W. 410.4



Cat. No. 444283 **1 mg** **€ 85**

Ref.: Engel, C.K., et al. 2005. *Chem. Biol.* **12,** 181.

MMP-13 Substrate, Fluorogenic

A quenched fluorescence substrate for MMP-13 (k_{cat}/K_m = 1.09 × 10^6 $M^{-1}s^{-1}$). Less efficient as a substrate for MMP-1 or MMP-8. *Purity: ≥98% by HPLC.* M.W. 1100.2

Cat. No. 444235 **1 mg** **€ 219**

Ref.: Knauper, V., et al. 1996. *J. Biol. Chem.* **271,** 1544.

Cathepsin B Substrate V, Fluorogenic

[Abz-GIVR~AK(Dnp)-OH]

An internally-quenched fluorogenic peptide substrate that is selectively and efficiently cleaved by human cathepsin B (k_{cat}/K_m in $M^{-1}s^{-1}$ at pH 4.5 = 7288, 133.3, 100 for cathepsin B, cathepsin K, cathepsin L, respectively). (Ex. max. = 320 nm, Em. max. = 420 nm). *Purity: ≥95% by HPLC.* M.W. 928

Cat. No. 219480 **5 mg** **€ 281**

Ref.: Cortrin, S.S., et al. 2004. *Anal. Biochem.* **335,** 244.

Kits for Proteomics Research

NEW iFOLD™ Protein Refolding System 1

The iFOLD™ Protein Refolding System 1 is a simple, reliable, and comprehensive method for identifying optimal protein refolding conditions. The kit provides a systematic evaluation of 92 buffers representing different combinations of pH, salt, cyclodextrin, redox agent, and refolding additives. The buffer matrix is based on extensive literature review of successful refolding experiments and information contained in the REFOLD database (http://refold.med.monash.edu.au). The system is comprised of inclusion body purification reagents and a pre-dispensed 96-well plate-based matrix of refolding buffers.

Cat. No. 71552-3 1 system € 315

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

Sample type: Mammalian tissues and cultured cells
This kit is suitable for the isolation of native integral membrane and membrane-associated proteins, without the need for ultracentrifugation. Extraction is based on association of proteins with cellular membranes rather than on their hydrophobicity. Resulting samples are suitable for use in functional assays, 2-D gel electrophoresis, and other applications.

Cat. No. 444810 1 kit € 280

ProteoExtract® Protein Precipitation Kit

A convenient and highly reproducible kit for the precipitation and clean-up of proteins. Yield of precipitated proteins is higher than that of traditional methods with improved solubility of the precipitated protein. Contains sufficient components to precipitate 200 samples of ≤200 µl. Kit delivers protein solutions of very low conductivity.

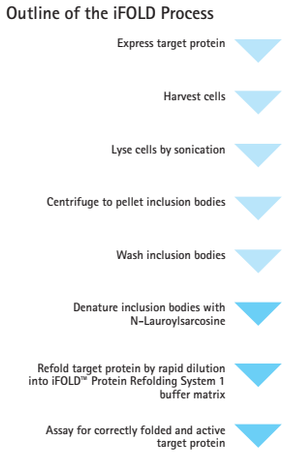
Cat. No. 539180 1 kit € 209

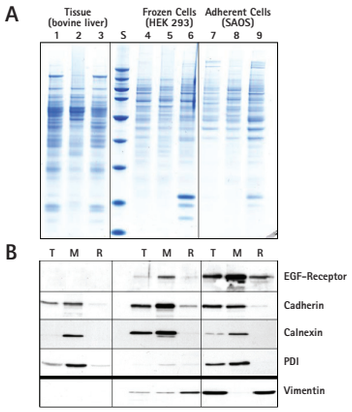
NEW ProteoExtract® Phosphoproteome Profiler Kit

Sample type: Fractionated proteome
A convenient and highly reproducible kit to measure the activation of signal transduction pathways controlled by protein phosphorylation patterns resulting from external and internal signaling. Contains sufficient components for 25 reactions.

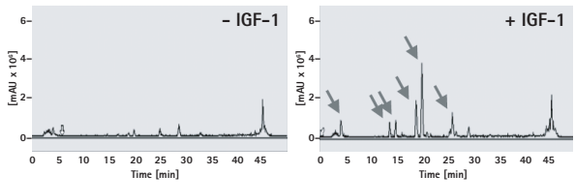
Cat. No. 539181 1 kit € 248

More online... www.calbiochem.com/proteoextract





Selective enrichment of membrane proteins from tissues and cells.
(A) 10 µg of each extracted fraction was separated using 10% Bis-Tris SDS-PAGE and visualized by Coomassie staining. The membrane protein patterns (lanes 2, 5, and 8) are distinct from the patterns of both total and non-membraneous fractions.The M.W. standards (lane S) represent bands at 225, 150, 75, 50, 25, 15, and 10 kDa.
(B) Immunoblots of equivalent gels using membrane-associated and integral membrane protein markers demonstrate the selectively of the M-PEK protocol. Following M-PEK extraction, all marker membrane proteins are enriched in the M fraction, whereas non-membrane proteins are depleted in the membrane fraction.



Phosphopeptide signal pattern of MCF-7 cells (membrane fraction) induced by IGF-1. 3×10^6 MCF-7 cells, serum starved for 24 h, were seeded in 75 cm^2 flasks in RPMI 1640. Cells were treated with 10 ng/ml of IGF-1 and membrane fractions were isolated using ProteoExtract® Native Membrane Protein Extraction Kit (Cat. No. 444810). Using the ProteoExtract® Phosphoproteome Profiler Kit (Cat. No. 539181),, 100 µg of each protein fraction was precipitated and digested with trypsin and phosphopeptide enrichment was performed using 40 µl of the digest. Phosphopeptide-enriched fractions were analyzed using ESI LC/MS using a Bruker Daltonics Esquire. IGF-1 induced phosphorylation of specific peptides is shown with arrows.

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Kits for Proteomics Research *continued...*

NEW ProteoEnrich™ CAT-X Kit

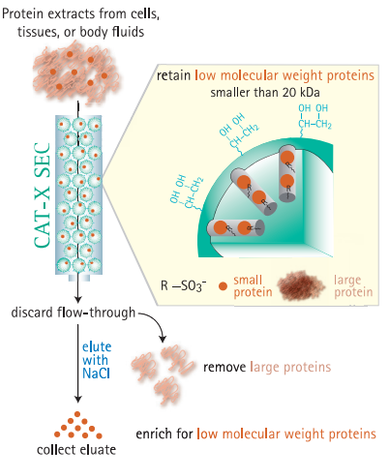
This kit provides a convenient and reproducible method to fractionate the proteome of a given biological sample under non-denaturing conditions prior to downstream analysis by one- and two-dimensional gel electrophoresis (2DGE), liquid chromatography, protein arrays, and functional tests. Proteins are fractionated based on their binding to the strong cation exchange resin, Fractogel® EMD SO_3. Nearly the complete proteome binds to the matrix under slightly acidic conditions, and partial proteomes can be eluted with a salt gradient. Excess salt should be removed prior to 2DGE. CAT-X cartridge included with the kit can bind up to 140 mg protein and can be reused at least 10 times.

Cat. No. 71532-3 **1 kit** **€ 133**

NEW ProteoEnrich™ CAT-X SEC Kit

This kit provides a highly specific method to enrich the proteome of a biological sample such as body fluids and crude tissue extracts for low molecular weight proteins. The method is based on a unique resin that allows proteins and polypeptides with a globular size of less than 20 kDa to penetrate the resin pores and bind to the surface of the inner pores according to their net charge while larger proteins flow through the resin-filled cartridge. After a salt gradient or single step elution and excess salt removal, the sample can be used for downstream analysis by mass spectrometry, SELDI, or array-based analysis. CAT-X SEC cartridge included with the kit can bind up to 10 mg complex protein mixture and can be reused at least 10 times.

Cat. No. 71539-3 **1 kit** **€ 159**

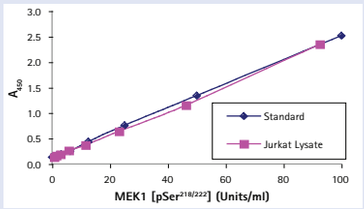


NEW Protein Kinase Assay Kits

PhosphoDetect™ MEK1 (pSer218/222) ELISA Kit

Sensitivity: ≤ 0.9 unit/ml
Assay range: 1.6–100 units/ml
Sample type: Cells
A convenient 96-well plate method, suitable for detection and quantitation of MEK1 dually phosphorylated at Ser^{218} and Ser^{222}. This kit is designed for use with human and mouse cells.

Cat. No. CBA030 **1 kit** **€ 704**

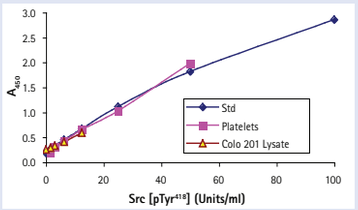


MEK1 ($pSer^{218/222}$) from PMA-treated Jurkat cell lysate was serially diluted in standard dilution buffer. Absorbance of each dilution was plotted against the MEK1 ($pSer^{218/222}$) standard curve. Demonstrated parallelism indicates that the standard accurately reflects MEK1 ($pSer^{218/222}$) content in the sample.

PhosphoDetect™ Src (pTyr418) ELISA Kit

Format: 96-well plate
Sensitivity: ≤ 1 unit/ml
Assay range: 1.6–100 units/ml
Sample type: Cells
Suitable for detecton and quantitation of c-Src protein that is phosphorylated at Tyr^{418}. Although this kit is designed for use with human cell lines, platelets, and lymphocytes, it cross-reacts with mouse and rat cells.

Cat. No. CBA028 **1 kit** **€ 704**



Src ($pTyr^{418}$) from extracts of platelets and Colo 201 cells in RPMI + 10% FCS was serially diluted in standard diluent buffer. Absorbance of each dilution was plotted against the Src ($pTyr^{418}$) standard curve. Parallelism demonstrated indicates that standard accurately reflects full length Src ($pTyr^{418}$) content in samples.

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NEW Protein Kinase Inhibitors

Chk2 Inhibitor

{5-(2-Amino-5-oxo-1,5-dihydroimidazol-4-ylidine)-3,4,5,10-2H-azepino[3,4-b]indol-1-one, HCl}

A cell-permeable, potent inhibitor of Chk2 (IC_{50} = 8 nM) that targets the ATP binding pocket. Exhibits selectivity for Chk2 over MEK1, Chk1, CK1δ, PKCα, $PKC_{βII}$, and CK2 (IC_{50} = 89 nM, 237 nM, 1.352 µM, 2.539 µM, 3.381 µM, and > 10.0 µM, respectively). *Purity: ≥95% by HPLC.* M.W. 331.8

Cat. No. 220485 **500 µg** **€ 219**

Ref.: Sharma, V., and Tepe, J.J. 2004. *Bioorg. Med. Chem. Lett.* **14,** 4319; Sharma, V., et al. 2004. *J. Med. Chem.* **47,** 3700.

Lck Inhibitor

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

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

Cat. No. 428205 **1 mg** **€ 72**

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

Rho Kinase Inhibitor III, Rockout

[3-(4-Pyridyl)-1H-indole]

A cell-permeable, selective, ATP-competitive inhibitor of Rho kinase (IC_{50} = 25 µM). Does not inhibit the activation of Rho kinase. *Purity: ≥98% by HPLC.* M.W. 194.2

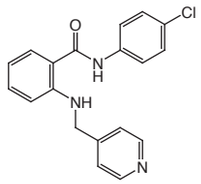
Cat. No. 555553 **10 mg** **€ 77**

Ref.: Yarrow, J.C., et al. 2005. *Chem. Biol.* **12,** 385.

VEGF Receptor Tyrosine Kinase Inhibitor II

{N-(4-Chlorophenyl)-2-[(pyridin-4-ylmethyl)amino]benzamide}

A potent inhibitor of the kinase activities of KDR, Flt-1, and c-Kit (IC_{50} = 20 nM, 180 nM, and 240 nM, respectively). Minimally inhibits c-Src and EGF-R activities (IC_{50} = 7.0 µM and 7.3 µM). *Purity: ≥98% by HPLC.* M.W. 337.8



Cat. No. 676481 **5 mg** **€ 149**

Ref.: Furet, P., et al. 2003. *Bioorg. Med. Chem. Lett.* **13,** 2967.

Ready-to-use, InSolution™ Protein Kinase Inhibitors

More online... www.calbiochem.com/insolution

Name	Cat. No.	Comments	Size	Price
InSolution™ AMPK Inhibitor, Compound C	171261	Supplied as a 10 mM (1 mg/250 µl) solution of AMPK Inhibitor, Compound C (Cat. No. 171260) in DMSO. *Purity:≥95% by HPLC.* M.W. 399.5	1 mg	€ 63
InSolution™ Casein Kinase I Inhibitor, D4476	218705	Supplied as a 10 mM (1 mg/251 µl) solution of Casein Kinase I Inhibitor, D4476 (Cat. No. 218696) in DMSO *Purity:≥95% by HPLC.* M.W. 398.4	1 mg	€ 143
InSolution™ Casein Kinase II Inhibitor, DMAT	218706	Supplied as a 10 mM (5 mg/1.05 ml) solution of Casein Kinase II Inhibitor, DMAT (Cat. No. 218699), in DMSO *Purity:≥95% by HPLC.* M.W. 476.8	5 mg	€ 106
InSolution™ GSK-3β Inhibitor VIII	361557	Supplied as a 25 mM (5 mg/649 µl) solution of GSK-3β Inhibitor VIII (Cat. No. 361549) in DMSO. *Purity:≥95% by HPLC.* M.W. 308.3	5 mg	€ 74
InSolution™ JAK Inhibitor I	420097	Supplied as a 10 mM (500 µg/162 µl) solution of JAK Inhibitor I (Cat. No. 420099) in DMSO. *Purity:≥98% by HPLC.* M.W. 309.3	500 µg	€ 99
InSolution™ p38 MAP Kinase Inhibitor III	506148	Supplied as a 10 mM (1 mg/247 µl) solution of p38 MAP Kinase Inhibitor III (Cat. No. 506121) in DMSO. *Purity:≥98% by HPLC.* M.W. 404.5	1 mg	€ 105
InSolution™ PD 158780	513036	Supplied as a 10 mM (500 µg/151 µl) solution of PD 158780 (Cat. No. 513035) in DMSO. *Purity:≥95% by HPLC.* M.W. 330.2	500 µg	€ 94
InSolution™ Rapamycin	553211	Supplied as a 5 mM (500 µg/109 µl) solution of Rapamycin (Cat. No. 553210) in DMSO. *Purity:≥98% by TLC.* M.W.914.2	500 µg	€ 112
InSolution™ Rho Kinase Inhibitor	555552	Supplied as a 10 mM (500 µg/128 µl) solution of Rho Kinase Inhibitor (Cat. No. 555550) in H_2O. *Purity:≥95% by HPLC.* M.W. 392.3	500 µg	€ 106
InSolution™ VEGF Receptor 2 Kinase Inhibitor III	676498	Supplied as a 10 mM (500 µg/210 µl) solution of VEGF Receptor 2 Kinase Inhibitor III (Cat. No. 676487) in DMSO. *Purity:≥95% by HPLC.* M.W. 238.3	500 µg	€ 86

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NEW Antibodies for Protein Kinase Research

Name	Cat. No.	Comments	Size	Price
Anti-JAK1 Rabbit pAb	PK1004	Protein A and immunoaffinity purified. Recognizes the ~130 kDa JAK1 protein in CTLL-2 and BaF3 cells. Reacts with human, mouse. **IB, IP, PS**	50 µl	€ 122
Anti-Lck Rabbit pAb	PK1105	Protein A and immunoaffinity purified. Recognizes the ~56 kDa Lck protein in calf intestinal alkaline phosphatase (CIP) and H_2O_2-treated Jurkat cells. Reacts with human, mouse. **FC, IB, IP**	50 µl	€ 122
Anti-Lyn Rabbit pAb	ST1107	Protein A and immunoaffinity purified. Recognizes the ~56 kDa form of Lyn in anti-IgM-treated Ramos cells. Does not recognize the ~53 kDa isoform of Lyn. Reacts with human, mouse, rat. **IB, IP, PS**	50 µl	€ 122
PhosphoDetect™ Anti-MAPKAPK-2 (pThr^{222}) Rabbit pAb	PK1007	Protein A and immunoaffinity purified. Recognizes the ~47 kDa MAP kinase-activated protein kinase 2 (MAPKAPK-2) protein phosphorylated at Thr^{222} in anisomycin-treated HeLa cells. Reacts with human, mouse, rat. **IB**	50 µl	€ 176
Anti-PAK4 Rabbit pAb	AP1019	Immunoaffinity purified. Recognizes the ~68 kDa PAK4 protein in HeLa and Jurkat cells. Reacts with human. **IB, IP**	50 µg	€ 149
Anti-PAK5 Rabbit pAb	ST1097	Immunoaffinity purified. Recognizes the ~85 kDa PAK5 protein in transfected CHO cells. Reacts with human. **IB, IC**	50 µg	€ 122
Anti-Pim1 Rabbit pAb	ST1091	Immunoaffinity purified. Detects the ~33 kDa Pim1 protein. Reacts with human. **IB, IP**	50 µg	€ 125
Anti-PKD3 Rabbit pAb	ST1090	Immunoaffinity purified. Detects the ~100 kDa PKD3. Reacts with human. **IB**	50 µg	€ 125
Anti-Plk1 Mouse mAb (35-206)	DR1037	Protein G purified. Recognizes the ~62 kDa Plk1 protein in HeLa cells. Reacts with human, mouse, rat. **IB, IP**	50 µg	€ 126
Anti-SLK Rabbit pAb	AP1039	Immunoaffinity purified. Recognizes the ~145 kDa human SLK (Ste20-like kinase) protein in HeLa cells. Reacts with human. **IB, IP**	50 µg	€ 122
Anti-STK10 Rabbit pAb	ST1093	Recognizes the ~130 kDa STK10 (Serine/Threonine kinase 10) in HeLa cells. Reacts with human. **IB, IH**	50 µg	€ 126

FC: flow cytometry; **IB**: immunoblotting; **IC**: immunocytochemistry; **IH:** immunohistochemistry; **IP**: immunoprecipitation; **PS**: paraffin sections

NEW Enzymatically Active Protein Kinases

Name	Cat. No.	Comments	Size	Price
Akt2, GST-Fusion Protein, Active, Human, Recombinant	124021	Active Akt2 with an N-terminal GST-fusion protein. Contains S473D and T308E mutations. Specific activity: ≥45 units/µg. *Purity:≥80% by SDS-PAGE.* M.W. 68,000	20 µg	€ 274
PKCι, GST-Fusion Protein, Active, Human, Recombinant, *S. frugiperda*	539685	A full-length recombinant human PKCι with an N-terminal GST-fusion protein. Specific activity: ≥565 nmol/min/mg. *Purity:≥90% by SDS-PAGE.* M.W. ~98,000	5 µg	€ 86
PKCµ, GST-Fusion Protein, Active, Human, Recombinant, *S. frugiperda*	539686	A full-length recombinant human PKCµ with an N-terminal GST-fusion protein. Specific activity: ≥560 nmol/min/mg. *Purity:≥90% by SDS-PAGE.* M.W. ~131,000	5 µg	€ 90
PKCν, GST-Fusion Protein, Active, Human, Recombinant, *S. frugiperda*	539687	A full-length recombinant human PKCν with an N-terminal GST-fusion protein. Specific activity: ≥67 nmol/min/mg. *Purity:≥80% by SDS-PAGE.* M.W. ~142,000	5 µg	€ 90
Raf1, GST-Fusion Protein, Active, Human, Recombinant, *S. frugiperda*	553012	A full-length recombinant human Raf1with an N-terminal GST-fusion protein. Specific activity: ≥90 nmol/min/mg. *Purity:≥90% by SDS-PAGE.* M.W. ~64,000	5 µg	€ 135
SGK1, GST-Fusion Protein, Active, Human, Recombinant, *S. frugiperda*	535851	Active recombinant human SGK1 (serum/glucocorticoid regulated kinase 1) protein amino acids 61-431, expressed with N-terminal GST-fusion protein. Specific activity: ≥55 nmol/min/mg. *Purity:≥95% by SDS-PAGE.* M.W. ~73,000	5 µg	€ 90
Src1, GST-Fusion Protein, Active, Human, Recombinant, *S. frugiperda*	539688	A full-length recombinant human Src1 with an N-terminal GST-fusion protein. Specific activity: ≥98 nmol/min/mg. *Purity:≥90% by SDS-PAGE.* M.W. ~85,000	5 µg	€ 90
ZAP70, GST-Fusion Protein, Active, Human, Recombinant, *S. frugiperda*	539689	A full-length recombinant human ZAP-70 with an N-terminal GST-fusion protein. Specific activity: ≥96 nmol/min/mg. *Purity:≥90% by SDS-PAGE.* M.W. ~96,000	5 µg	€ 90

NEW Antibody for Stem Cell Research

Anti-Nanog Rabbit pAb

Immunoaffinity purified, provided at 1 mg/ml. Recognizes the ~40 kDa Nanog protein in mouse myeloid and embryonic stem cells. Nanog is a homeodomain transcription factor involved in embryonic stem cell renewal, maintenance of pluripotency, and epiblast formation. Reacts with mouse. Suitable for immunoblotting and immunoprecipitation.

Cat. No. SC1000 50 µg € 126

NEW Alzheimer's Disease Research Tools

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FSB

[*(E,E)*-1-Fluoro-2,5-*bis*(3-hydroxycarbonyl-4-hydroxy)styrylbenzene]

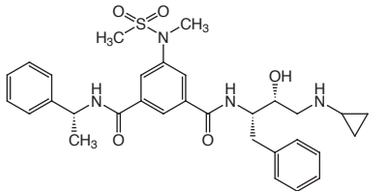
A fluorine analog of the amyloidophilic fluorescent probe BSB (Cat. No. 286895) that crosses the blood-brain barrier. Suitable for non-invasive amyloid visualization in living transgenic Tg2576 mice by using ^{19}F and ^{1}H-MRI. Useful for staining plaques and neurofibrillary tangles in brain tissue sections of Alzheimer's diseased patients with improved sensitivity, and reduced background.
Purity: ≥95% by NMR and HPLC.M.W. 420.4

Cat. No. 344101 **5 mg** **€ 167**

Ref.: Higuchi, M., et al. 2005. *Nat. Neurosci.* **8,** 527; Sato, K., et al. 2004. *Eur. J. Med. Chem.* **39,** 573.

β-Secretase Inhibitor IV

A cell-permeable inhibitor that binds to BACE-1 active site and potently blocks its proteolytic activity (IC_{50} = 15 nM for BACE-1, human and 29 nM for sAPP_NF in HEK293-APP^{NFEV} cells). Displays greater selectivity over other aspartyl proteases (IC_{50} = 230 nM, 7.6 µM, and > 50 µM for BACE-2, cathepsin D, and renin, respectively). *Purity: ≥95% by HPLC*. M.W. 578.7



Cat. No. 565788 **1 mg** **€ 172**

Ref.: Stachel, S.J., et al. 2004. *J. Med. Chem.* **47,** 6447.

γ-Secretase Inhibitor XX

{(S,S)-2-[2-(3,5-Difluorophenyl)acetylamino]-N-(5-methyl-6-oxo-6,7-dihydro-5H-dibenzo[b,d]azepin-7-yl)propionamide}

A cell-permeable, potent inhibitor of γ-secretase that significantly lowers brain and plasma $A\beta_{40}$ levels in Tg2576 mutant APP transgenic mouse model (100 µmol/kg, b.i.d). Also blocks Notch processing (IC_{50} = 1.7 nM in SupT1 cells). *Purity: ≥95% by HPLC*. M.W. 463.4

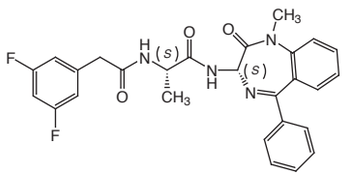
Cat. No. 565789 **500 µg** **€ 167**

Ref.: van Es, J.H., et al. 2005. *Nature* **435,** 959; Milano, J., et al. 2004. *Toxicol. Sci.* **82,** 341

γ-Secretase Inhibitor XXI

{(S,S)- 2-[2-(3,5-Difluorophenyl)-acetylamino]-N-(1-methyl-2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-propionamide; Compound E}

A cell-permeable, selective, peptidomimetic, non-transition-state analog inhibitor of γ-secretase and Notch processing (IC_{50} = 300 pM for $A\beta_{40}$ in CHO cells overexpressing wild type βAPP; 240 pM for $A\beta_{40}$, 370 pM $A\beta_{42}$, and 320 pM for NICD, respectively, in HEK293 cells stably transfected with βAPP_{695} and mNotchΔE(M1727V); 100 pM for both $A\beta_{40}$ and $A\beta_{42}$ in SH-SY5Y cells stably transfected with SPA4CT). *Purity: ≥95% by HPLC*.
M.W. 490.5



Cat. No. 565790 **500 µg** **€ 167**

Ref.: Jung, K. M., et al. 2003. *J. Biol. Chem.* **278,** 42161; Murakami, D., et al. 2003. *Oncogene* **22,** 1511; Campbell, W. A., et al. 2003. *J. Neurochem.* **85,** 1563; May, P., et al. 2002. *J. Biol. Chem.* **277,** 18736; Berechid, B. E., et al., 2002. *J. Biol. Chem.* **277,** 8154; Beher, D., et al. 2001. *J. Biol. Chem.* **276,** 45394; Seiffert, D., et al. 2000. *J. Biol. Chem.* **275,** 34086.

Neurochemicals

SNAP/Synaptotagmin Antibodies

Name	Cat. No.	Comments	Size	Price
Anti-SNAP-25 (195-206) Rabbit pAb	NE1014	Undiluted serum. Recognizes the ~25 kDa SNAP-25 protein in mouse and rat brain tissue extracts. Reacts with mouse, rat. **IB, IP**	100 µl	€ 266
PhosphoDetect™ Anti-Synaptotagmin (pSer^{309}) Rabbit pAb	PS1002	Immunoaffinity purified. Recognizes the ~60-62 kDa synaptotagmin protein phosphorylated on Ser^{309}. Reacts with human, mouse, rat. **DB, IB**	100 µl	€ 325
PhosphoDetect™ Anti-Synaptotagmin (pThr^{202}) Rabbit pAb	PS1006	Immunoaffinity purified. Recognizes the ~60-62 kDa synaptotagmin protein phosphorylated on Thr^{202}. Reacts with human, mouse, rat. **DB, IB**	100 µl	€ 325

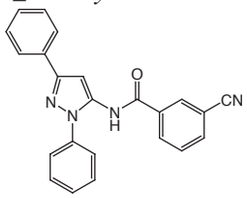
DB: dot blotting; **IB**: immunoblotting; **IP**: immunoprecipitation

Neurochemicals *continued...*

mGluR5 Ligand, CDPPB

[3-Cyano-N-(1,3-diphenyl-1H-pyrazol-5-yl)benzamide]

A pyrazole amide compound that crosses the blood-brain barrier and acts as a potent, selective, reversible, positive allosteric modulator for metabotropic glutamate receptor subtype 5. *Purity: ≥95% by HPLC.* M.W. 364.4



Cat. No. 445865 **1 mg** **€ 86**

Ref.: Kinney, G.G., et al. 2005. *J. Pharmacol. Exp. Ther.* **313,** 199; Lindsley, C.W., et al. 2004. *J. Med. Chem.* **47,** 5825.

mGluR5 Antagonist, MTEP

[3-((2-Methyl-1,3-thiazol-4-yl)ethynyl)pyridine]

A potent, selective and non-competitive mGluR5 antagonist (IC_{50} = 5 nM in Ca^{2+}-flux assay; K_i = 16 nM) with *in vivo* anxiolytic activity in rodent model (ED_{50} = 1 mg/kg, ip and 7 mg/kg, po). Does not exhibit any side effects seen with MPEP and benzodiazepines. *Purity: ≥98% by NMR.* M.W. 200.3

Cat. No. 445874 **5 mg** **€ 104**

Ref.: Bradbury, M.J., et al. 2005. *J. Pharmacol. Exp. Ther.* **313,** 395; Busse, C.S., et al. 2004. *Neuropsychopharmacology* **29,** 1971; Klodzinska, A., et al. 2004. *Neuropharmacology* **47,** 342; Brodkin, J., et al. 2002. *Eur. J. Neurosci.* **16,** 2241.

Polyglutamine Aggregation Inhibitor III, C2-8

[N-(4-Bromophenyl)-3-(((4-bromophenyl)amino)sulfonyl) benzamide]

A cell-permeable, potent inhibitor of polyglutamine (polyQ)-aggregation in Huntington's disease (HD); CA1 neuronal hippocampal slices in the range of 0.1 µM to 10 µM, and Htt-103Q-EGFP PC12 cells with an IC_{50} of 50 nM. Suggested to block the polymerization step of the polyQ aggregation. *Purity: ≥95% by HPLC.* M.W. 510.2

Cat. No. 528887 **10 mg** **€ 143**

Ref.: Zhang, X., et al. 2005. *Proc. Natl. Acad. Sci. USA* **102,** 892.-

(-)-Deguelin, *Mundulea sericea*

A cell-permeable, potent inhibitor of mitochondrial bioenergetics (IC_{50} = 6.9 nM for NADH:ubiquinone oxidoreductase activity in bovine heart ETP). Promotes mitochondrial permeability transition. Selectively blocks Akt activation with minimal effects on MAPK signaling. Also shown to activate AMPK activity and inhibit COX2 expression. *Purity: ≥98% by TLC.* M.W. 394.4

Cat. No. 252740 **5 mg** **€ 59**

Ref.: *Merck Index* **13,** 2883; Gills, J.J., et al. 2005. *J. Chemother.* **17,** 297; Hail, N. Jr., and Lotan, R. 2004. *Apoptosis* **9,** 437; Lee, H.Y., et al. *Clin. Cancer Res.* 2004. **10,** 1074; Fang, N., and Casida, J.E. 1998. *Proc. Natl. Acad. Sci. USA* **95,** 3380; Gerhauser, C., et al. 1995. *Nat. Med.* **1,** 260.

NEW Inhibitors for Apoptosis Research

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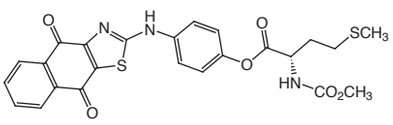
Bcl-2 Inhibitor II, YC137

{2-Methoxycarbonylamino-4-methylsulfanyl-butyric acid, 4-(4,9-dioxo-4,9-dihydronaphtho[2,3-d]thiazol-2-ylamino)-phenyl ester}

A cell-permeable, selective inducer of apoptosis in Bcl-2-overexpressing cells (< 300 nM in MDA-MB435B breast cancer cells) with little effect on a variety of primary cells, and Bcl-x_L-dependent cells, even at a concentration of 5 µM. Preferentially binds Bcl-2 (K_i = 1.3 µM) and disrupts its interaction with Bid BH3. Shown to induce the release of cytochrome *c* from mitochondria and activate caspase-9. *Purity: ≥95% by HPLC.* M.W. 511.6



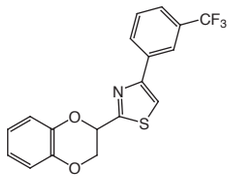
Cat. No. 197331 **5 mg** **€ 165**

Ref.: Real, P.J., et al. 2004. *Cancer Res.* **64,** 7947.

Caspase Inhibitor X

(BI-9B12)

A benzodioxane containing 2,4-disubstituted thiazolo compound that acts as a selective, reversible, and competitive inhibitor of caspases (K_i = 4.3 µM, 6.2 µM, and 2.7 µM for caspase-3, -7, and -8, respectively). The benzodioxane moiety is shown to fit in the 'aspartate hole' of the caspases and possibly disrupt caspase-8 assisted cleavage of BID. *Purity: ≥97% by HPLC.* M.W. 363.4



Cat. No. 218723 **5 mg** **€ 141**

Ref.: Fattorusso, R., et al. 2005. *J. Med. Chem.* **48,** 1649.

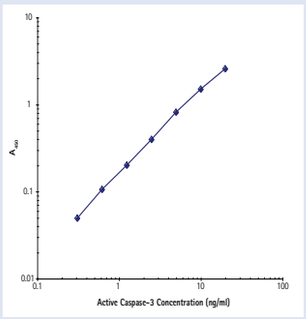
NEW Apoptosis Detection Kits

Discover our Apoptosis Kits Selection Guide: www.calbiochem.com/apoptosiskits

Active Caspase-3 ELISA Kit

Format: 96-well plate
Sample type: Cells
This ELISA assay kit measures active caspase-3 in cell extracts. This kit uses a biotinylated caspase inhibitor to covalently modify the large subunit of active caspase-3. Specific detection of active caspase-3 is achieved by quantitative sandwich ELISA. Assay is suitable for use with human and mouse samples.

Cat. No. CBA045 **1 kit** **€ 485**



Active Caspase-8 Assay Kit

Format: 96-well plate
Sample type: Cells
This is a convenient immunofluorescent assay for the quantitative detection of active caspase-8 in cell lysates. This kit captures active caspase-8 using a caspase-8 specific antibody. Active caspase-8 cleaves and activates procaspase-3, which in turn cleaves AFC from DEVD-AFC to generate fluorescence.

Cat. No. CBA046 **1 kit** **€ 383**

Active Caspase-9 Assay Kit

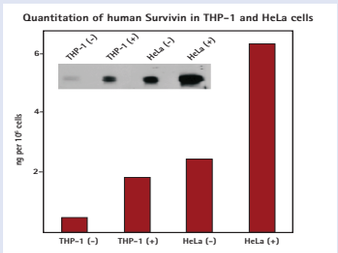
Format: 96-well plate
Sample type: Cells
This is a convenient immunofluorescent assay for the quantitative detection of active caspase-9 in cell lysates. This kit captures active caspase-9 complexed with APAF-1. Active caspase-9 cleaves and activates procaspase-3, which in turn cleaves AFC from DEVD-AFC to generate fluorescence.

Cat. No. CBA047 **1 kit** **€ 383**

Survivin ELISA Kit

Format: 96-well plate
Sample type: Cells
This ELISA detects and quantifies native and recombinant human Survivin in cell lysates. An immobilized capture antibody binds survivin in samples and standards.

Cat. No. CBA048 **1 kit** **€ 383**



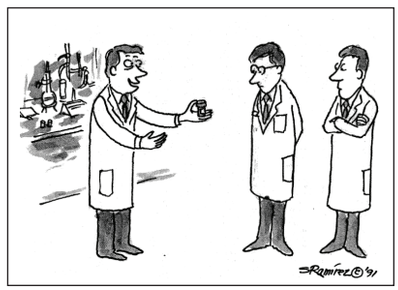
THP-1 and HeLa cells were either untreated or treated with 200 ng/ml nocodazole for 16 h. Survivin was measured using the Survivin ELISA Kit (Cat. No. CBA048). The same lysates were immunoblotted with rabbit anti-human Survivin. The ELISA results correlate well with the amounts of Survivin detected by immunoblotting.

Apoptosis-Inducing Factor (AIF), Human, Recombinant, *E. coli*

A mitochondrial flavoprotein that plays a major role in caspase-independent apoptosis. Useful for DNA binding studies, DNA fragmentation studies, protein-protein interaction, immunoblotting, and cell-free apoptosis experiments. *Purity: ≥95% by SDS-PAGE.* M.W. 62,000

Cat. No. 123042 **50 µg** **€ 312**

Ref.: Hong, S.J., et al. 2004. *Trends Pharmacol. Sci.* **25,** 259; Cregan, S.P., et al. 2002. *J. Cell. Biol.* **158,** 507; Ye, H., et al. 2002. *Nat. Struct. Biol.* **9,** 680; Yu, S. W., et al. 2002. *Science* **297,** 259.



"This antibiotic has the power to induce an enormous amount of stress on bacteria, the equivalent to 20 years of daily commuting on your average freeway."

Antibodies for Apoptosis Research

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Anti-Cleaved Caspase-3 (Asp^{175}) Rabbit pAb

Protein A and immunoaffinity purified. Recognizes the ~17-19 kDa large fragment of cleaved caspase-3. Does not recognize full-length caspase-3 or other cleaved caspases. Reacts with human, mouse, rat. Suitable for flow cytometry, free floating sections, immunoblotting, immunocytochemistry, and paraffin sections.

Cat. No. AP1027 **50 µl** **€ 195**

Anti-Cleaved Caspase-9 (Asp^{353}) Rabbit pAb

Protein A and immunoaffinity purified. Recognizes the ~37 kDa cleaved caspase-9 resulting from cleavage adjacent to Asp^{353}. Does not recognize full-length or other cleaved caspases. Reacts with mouse. Suitable for immunoblotting and immunocytochemistry.

Cat. No. AP1028 **50 µl** **€ 195**

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

Undiluted ascites. Recognizes the ~45 kDa latent form of caspase-1 in HeLa cells. Also recognizes cleaved forms of caspase-1 that retain amino acids 31-45. Reacts with human. Suitable for immunoblotting and immunocytochemistry.

Cat. No. AP1044 **50 µg** **€ 149**

Anti-Caspase-1 Mouse mAb (14F468)

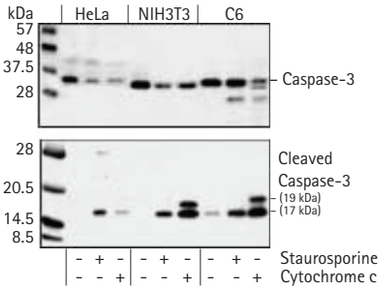
Protein G purified. Recognizes the ~45 kDa latent form of caspase-1 in HeLa and NIH3T3 cells. Also recognizes cleaved forms of caspase-1 that retain amino acids 371-390. Reacts with human, mouse. Suitable for immunoblotting and immunohistochemistry on paraffin sections.

Cat. No. AP1043 **50 µg** **€ 167**

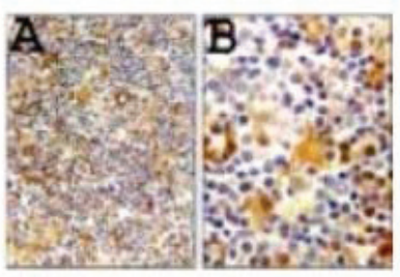
Anti-p53 Binding Protein 1 Mouse mAb (BP13)

Recognizes the ~230 kDa 53BP1 protein in HeLa nuclear extract (Cat. No. WB64) and HEK293 whole cell lysate. Reacts with human. Suitable for immunoblotting, immunocytochemistry, and immunoprecipitation.

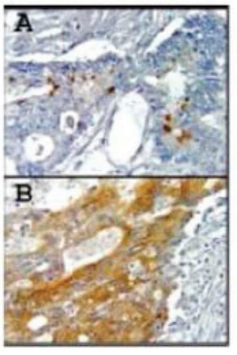
Cat. No. DR1003 **50 µl** **€ 164**



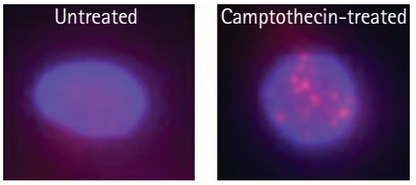
Detection of human, mouse, and rat cleaved caspase-3. Lysates from untreated and Staurosporine-treated or cytochrome c treated (250 µg/ml) HeLa, NIH/3T3, and C6 cells were used. Primary antibody: Anti-Caspase-3 (Upper) and Anti-Cleaved Caspase-3 (Asp^{175}) (Cat. No. AP1027) (1:1000) (lower). Detection: chemiluminescence.



Detection of human caspase-1 in paraffin sections. Sample: Formalin fixed lymph node. Primary antibody: Anti-caspase-1 (31-45) Rabbit pAb (Cat. No. AP1044). Detection: DAB with hematoxylin counter stain.



Detection of human caspase-1 in paraffin sections. Sample: Formalin fixed colon carcinoma. Primary antibody: Anti-caspase-1 Mouse mAb (14F468) (Cat. No. AP1043). Detection: DAB with hematoxylin counter stain.



Detection of human 53BP1 by immunofluorescence. Sample: Untreated and camptothecin treated (12 ng/ml) HeLa cells fixed with 1% paraformaldehyde and permeabilized with 0.2% TRITON®-X 100. Primary antibody: Anti-p53 Binding Protein 1 (BP13) (Cat. No. DR1003) (1:300). Secondary antibody: Goat anti-mouse conjugated to Alexa Fluor® 546. Detection: fluorescence, P53BP1 (red) and DAPI (blue).

NEW Protein Phosphatases

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

Full-length human PTEN (phosphatase and tensin homolog deleted on chromosome 10) containing an N-terminal His•Tag® sequence and an S•Tag™ sequence expressed in and purified from *Spodoptera frugiperda* insect cells. Specific activity: ≥75 units/mg protein. One unit is defined as the amount of enzyme required to liberate 1.0 nmol phosphate from PIP_3 per minute at 37°C. *Purity: ≥80% by SDS-PAGE.* M.W. 53,000

Cat. No. 481409 **10 µg** **€ 270**

Ref.: Harrington, L.S., et al. 2005. *Trends Biochem. Sci.* **30,** 35; Osaki, M., et al. 2004. *Apoptosis* **9,** 667; Lennon, G., et al. 1996. *Genomics* **33,** 151.

PTP-MEG2, GST-Fusion Protein, Human, Recombinant, *E. coli*

(Protein tyrosine phosphatase, non-receptor type 9; PTPase-MEG2; PTPN9)

Recombinant catalytic domain of human MEG2 protein tyrosine phosphatase consisting of amino acids 285-593 fused to GST at the N-terminus, expressed in and purified from *E. coli*. PTP-MEG2 is an intracellular tyrosine phosphatase that contains a Sec14 homology domain. Useful for studies involving enzyme kinetics, regulation, and inhibitor screening. Specific activity: ≥1 unit/µg protein. One unit is defined as the amount of enzyme that will hydrolyze 1.0 nmol of *p*NPP per minute at 30°C. M.W. 60,300

Cat. No. 535857 **20 µg** **€ 214**

Ref.: Huynh, H., et al. 2003. *J. Immunol.* **171,** 6661; Qi, Y., et al. 2002. *J. Cell Biochem.* **86,** 79.

Antibodies for PTEN

Name	Cat. No.	Comments	Size	Price
Anti-PTEN (188-403) Sheep pAb	PC623	Immunoaffinity purified. Recognizes the ~54 kDa PTEN protein. Reacts with human. **IB**	250 µg	€ 285
Anti-PTEN Mouse mAb (EMD-15E10)	AP1041	Protein G Plus/Protein A purified. Recognizes the ~55 kDa PTEN protein in MCF-7 cells. Reacts with human. **ELISA, IP, NOT IB**	50 µg	€ 122
Anti-PTEN Mouse mAb (EMD-4B8)	AP1042	Protein G Plus/Protein A purified. Recognizes the ~55 kDa PTEN protein in MCF-7 cells. Reacts with human. **IB, NOT IP**	50 µg	€ 122

ELISA: enzyme-linked immunosorbent assay; **IB**: immunoblotting; **IP**: immunoprecipitation

NEW Lipase Activator and Inhibitor

Lipoprotein Lipase Activator

[Diethyl-4-((4-Bromo-2-cyanophenyl)carbamoyl)benzylphosphonate; NO-1886]

A cell-permeable selective inducer of lipoprotein lipase (LPL) mRNA and protein levels. Does not exhibit PPARα or PPARγ agonistic activities. Lowers serum lipid levels and plasma triglycerides with concomitant elevation in HDL-C in animal models. Induces fatty acid oxidation. *Purity: ≥95% by HPLC.* M.W. 451.3

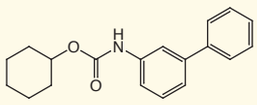
Cat. No. 437704 **5 mg** **€ 86**

Ref.: Niho, N., et al. 2005. *Proc, Natl. Acad. Sci. USA* **102,** 2970; Yin, W., et al. 2004. *Pharmacol. Res.* **49,** 199; Doi, M., et al. 2003. *Metabolism* **52,** 1547; Kusunoki, M., et al. 2000. *Diabetologia*; **43,** 875; Tsutsmi, K., et al. 1993. *J. Clin. Invest.* **92,** 411.

Monoacylglycerol Lipase Inhibitor, URB602

(N-Biphenyl-3-ylcarbamic acid, cyclohexyl ester)

A cell-permeable, selective, and non-competitive inhibitor of monoacylglycerol lipase (MGL; IC_{50} = 28 µM for rat brain). Does not inhibit the activities of diacylglycerol lipase, FAAH, and COX-2. *Purity: ≥98% by HPLC and TLC.* M.W. 295.4



Cat. No. 475740 **10 mg** **€ 86**

Ref.: Hohmann, A.G., et al. 2005. *Nature* **435,** 1108.

Purified Small GTPases

Rac1, GST-Fusion, Human, Recombinant, *E. coli*

A small GTPase of the Ras superfamily that regulates lamellipodia formation in response to growth factor stimulation. Activates NADPH-oxidase in phagocytic lymphocytes and the JNK-MAP kinase cascade. Useful as a positive control in Western blotting and as an affinity precipitation reagent using immobilized glutathione (GST) resin. *Purity: ≥90% by SDS-PAGE.* M.W. 48,451

Cat. No. 552134 **10 µg** **€ 150**

Ref.: Kuroda, S., et al. 1996. *J. Biol. Chem.* **271,** 23363; Lamarche, N., et al. 1996. *Cell* **87,** 519; Ridley, A.J., et al. 1992. *Cell* **70,** 401.

Rac1, His•Tag®, Human, Recombinant, *E. coli*

A small GTPase of the Ras superfamily that regulates lamellipodia formation in response to growth factor stimulation. Activates NADPH-oxidase in phagocytic lymphocytes. Useful as a positive control in Western analysis and as an affinity precipitation reagent using Ni^{2+}-charged metal chelate resin. *Purity: ≥90% by SDS-PAGE.* M.W. 22,151

Cat. No. 552137 **10 µg** **€ 150**
25 µg **€ 322**

Ref.: Zhao, X., et al. 2003. *J. Biol. Chem.* **278,** 40788; Lamarche, N., et al. 1996. *Cell* **87,** 519; Ridley, A.J., et al. 1992. *Cell* **70,** 401.

NEW Recombinant Active Phosphodiesterases

cAMP and cGMP, two important second messenger molecules, are hydrolyzed by Phosphodiesterases (PDEs) in the cell, leading to cessation of cAMP and cGMP dependent effects. Phosphodiesterases (PDEs) comprise a large group of enzymes organized into 11 distinct families based on biochemical and molecular properties. Many of these isozymes are differentially expressed and regulated in different cells and exhibit distinct selectivity for cAMP and cGMP.

PDEs contain three functional domains: a regulatory N-terminus, a central catalytic domain, and a regulatory C-terminus. All isozymes exhibit significant homology in their catalytic domain. The N- and C-terminal domains also display moderate homology within families and impart specific characteristics to different subtypes. The N-terminus is involved in allosteric regulation and membrane targeting. The C-terminus is believed to be involved in dimerization and possess docking sites for PDE-specific kinases.

Due to their involvement in inflammation, asthma, and cardiovascular complication, PDEs are considered to be attractive targets for pharmacological intervention. A number of PDE inhibitors have been developed that target specific isoenzymes, thereby increasing tissue selectivity and minimizing side effects.

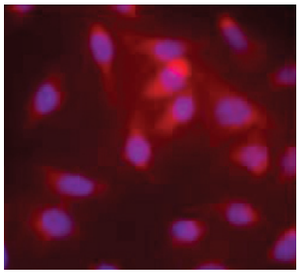
Name	Cat. No.	Comments	Size	Price
Phosphodiesterase 11A1, Active, Human, Recombinant, *S. frugiperda*	524735	A full-length, partially purified, catalytically active human PDE 11A1 expressed in *Spodoptera frugiperda*. Activity: ≥0.5 units/µl.	10 U	€ 203
Phosphodiesterase 3B, Active, Human, Recombinant, *S. frugiperda*	524734	A full-length, partially purified, catalytically active human PDE 3B expressed in *Spodoptera frugiperda*. Activity: ≥0.5 units/µl.	10 U	€ 203
Phosphodiesterase 4D3, Active, Human, Recombinant, *S. frugiperda*	524733	A full-length, partially purified, catalytically active human PDE 4D3 expressed in *Spodoptera frugiperda*. Activity: ≥0.5 units/µl.	10 U	€ 203
Phosphodiesterase 4A4, Active, Human, Recombinant, *S. frugiperda*	524731	A full-length, partially purified, catalytically active human PDE 4A4 expressed in *Spodoptera frugiperda*. Activity: ≥0.5 units/µl.	10 U	€ 203
Phosphodiesterase 4B2, Catalytic Domain, His•Tag®, Human, Recombinant, *S. frugiperda*	524732	A partially purified catalytic domain of human PDE 4B2 expressed in *Spodoptera frugiperda*. Activity: ≥0.5 units/µl.	10 U	€ 203
Phosphodiesterase 3A1, Catalytic Domain, Human, Recombinant, *S. frugiperda*	534736	The catalytic domain of human PDE 3A1 expressed in *Spodoptera frugiperda*. Activity: ≥0.5 units/µl.	10 U	€ 203

NEW Antibodies for Heat Shock Proteins

Anti-Hsp27 Mouse mAb (EMD-35)

Protein G Plus/Protein A purified, provided at 1 mg/ml. Recognizes the ~27 kDa Hsp27 (heat shock protein 27) in HeLa cells. Reacts with human. Suitable for ELISA, immunoblotting, immunocytochemistry, and immunoprecipitation.

Cat. No. CA1025 **50 µg** **€ 126**

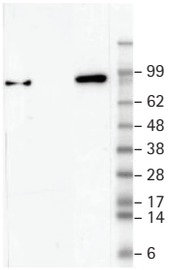


Detection of human Hsp27 by immunocytochemistry. Sample: HeLa cells fixed with 100% methanol. Primary antibody: Anti-Hsp27 Mouse mAb (EMD-35) (Cat. No. CA1025) (3 µg/ml). Detection: fluorescence with DAPI counterstain.

Anti-Hsp90α Mouse mAb (EMD-17D7)

Protein G Plus/Protein A purified, provided at 0.5 mg/ml. Recognizes the ~90 kDa Hsp90α protein in HeLa cells. Does not recognize Hsp90β. Reacts with human. Suitable for ELISA, immunoblotting, and immunoprecipitation.

Cat. No. CA1023 **50 µg** **€ 154**

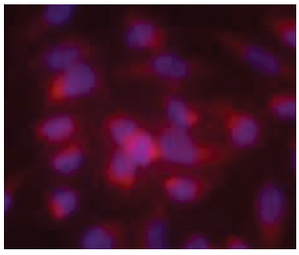


Detection of human Hsp90α. Sample: HeLa cell lysate (lane A; 50 µg), Hsp90β, His•Tag®, Human recombinant (Cat. No. 385903) (lane B: 100 ng); and Hsp90α, His•Tag®, Human, Recombinant (Cat. No. 385901) (lane C; 100 ng). Primary antibody: Anti-Hsp90α Mouse mAb (EMD-17D7) (Cat. No. CA1023) (1 µg/ml). Detection: chemiluminescence.

Anti-Hsp90β Mouse mAb (EMD-5E12)

Protein G Plus/Protein A purified, provided at 0.68 mg/ml. Recognizes the ~90 kDa Hsp90β protein in HeLa cells. Does not recognize Hsp90α. Reacts with human. Suitable for ELISA, immunoblotting, immunocytochemistry, and immunoprecipitation.

Cat. No. CA1024 **50 µg** **€ 154**



Detection of human Hsp90β by immunocytochemistry. Sample HeLa cells fixed in 100% methanol. Primary antibody: Anti-Hsp90β Mouse mAb (EMD-5E12) (3 µg/ml). Detection: fluorescence with DAPI counterstain.

Aurora-A Related Research Tools

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

Human full-length Aurora A (amino acids 1-403) was expressed in *Spodoptera frugiperda* insect cells with N-terminal His•Tag® and S•Tag™ sequences. Specific activity: ≥500 units/mg protein. *Purity: ≥80% by SDS-PAGE.* M.W. 51,000

Cat. No. 481410 **10 µg** **€ 270**

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

NEW Anti-Aurora-A Mouse mAb (35C1)

Protein G purified, provided at 1 mg/ml. Recognizes the ~48 kDa Aurora-A protein in HeLa cells. Reacts with human, mouse. Suitable for immunoblotting.

Cat. No. PK11 **50 µg** **€ 154**

Anti-Aurora-A Rabbit pAb

Immunoaffinity purified, provided at 1 mg/ml. Recognizes the ~48 kDa Aurora-A in HEK293 and BT474 cells. Reacts with human. Suitable for immunoprecipitation and immunohistochemistry (paraffin sections).

Cat. No. PC742 **100 µl** **€ 324**

Detection of human Aurora-A: Sample: 50 µg of HeLa cell lysates. Primary antibody: Anti-Aurora-A Mouse mAb (35C1) (Cat. No. PK11; 1 µg/ml). Detection: chemiluminescence.

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