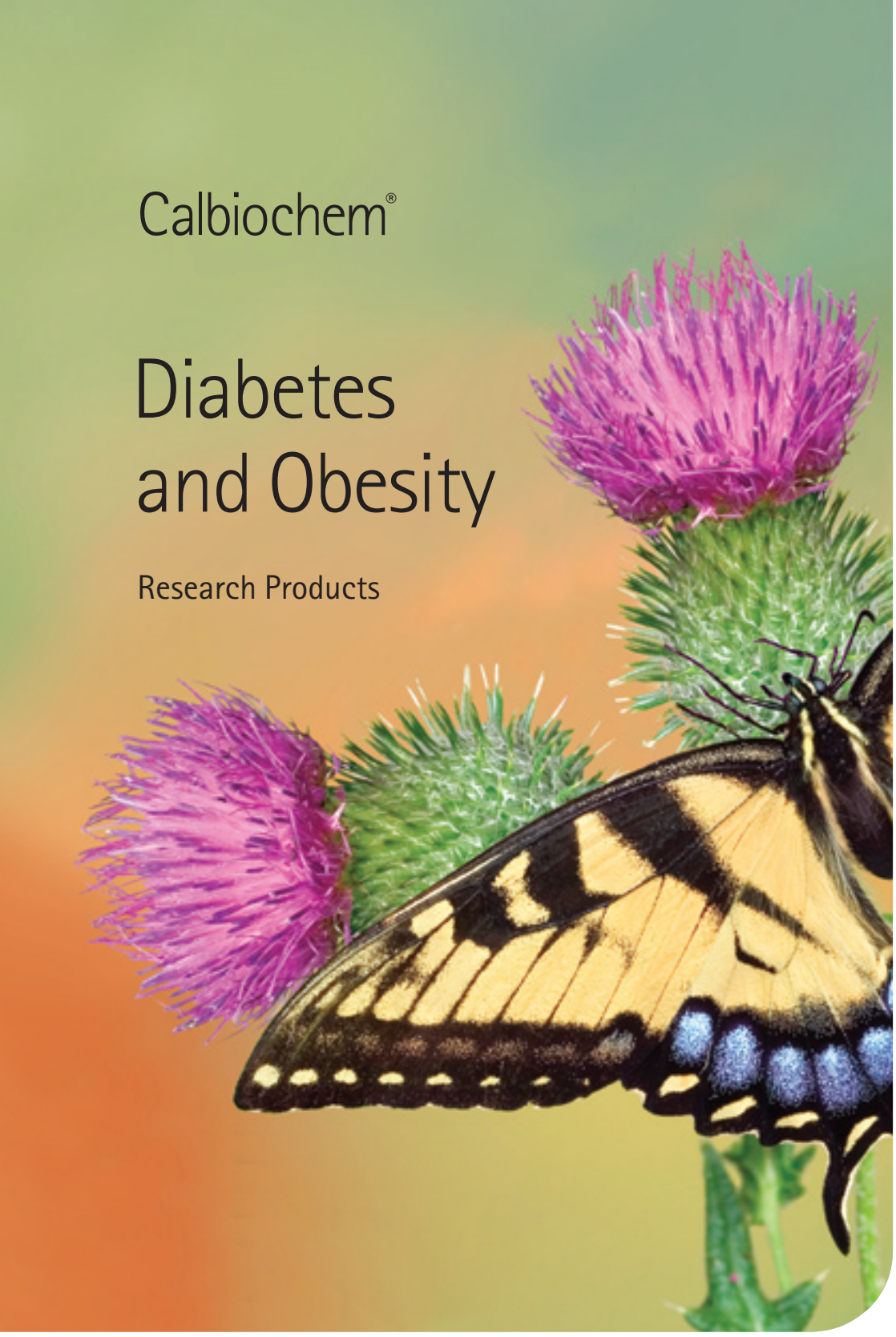
Calbiochem®

Diabetes and Obesity

Research Products



MERCK

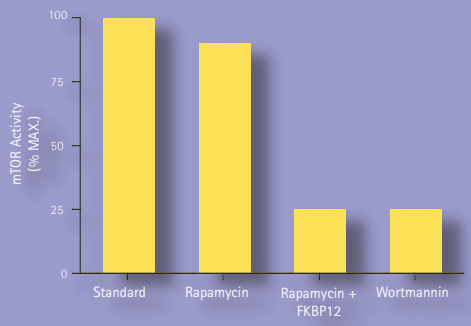
Calbiochem®

mTOR Signaling

Linking cell growth & survival with cancer

Advance your cancer research with the K-LISA™ mTOR Activity Kit from Calbiochem®, your exclusive provider of mTOR kinase and related tools. Assay features:

- Non-radioactive, 96-well format
- Active mTOR, isolated using proprietary methods
- Optimized for inhibitor screening

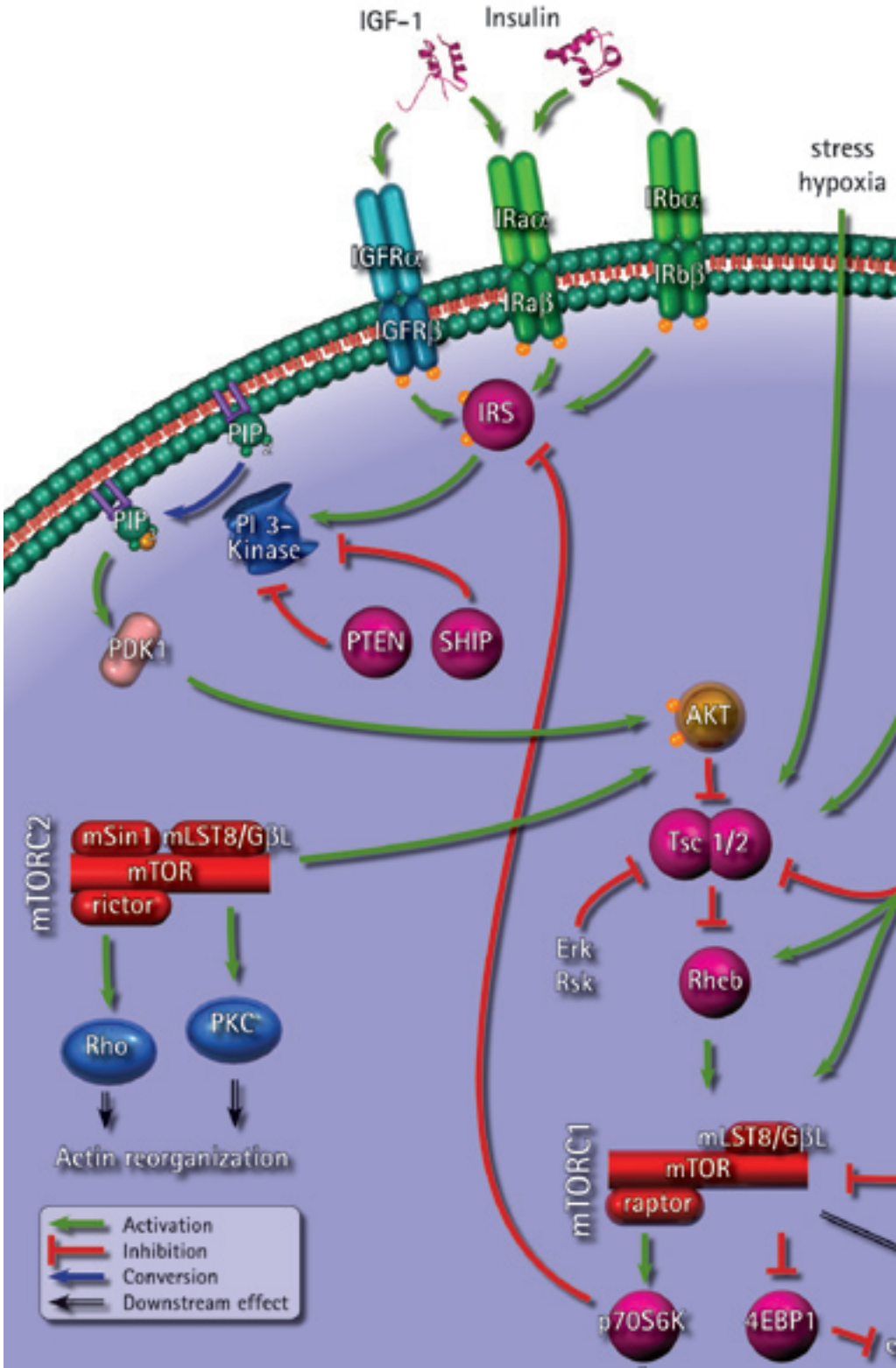


Rapamycin + FKBP12 inhibition of mTOR standard using the K-LISA mTOR Activity Kit (Cat. No.CBA055). Wortmannin is provided as an inhibitor of the PI-3 kinase pathway.

Visit **www.calbiochem.com/mTOR**

to view our portfolio of mTOR pathway assays, inhibitors, antibodies, and enzymes.

For more information or to place an order, contact your local office (see back cover).



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Diabetes, Obesity, Dyslipidemia, and Hypertension:

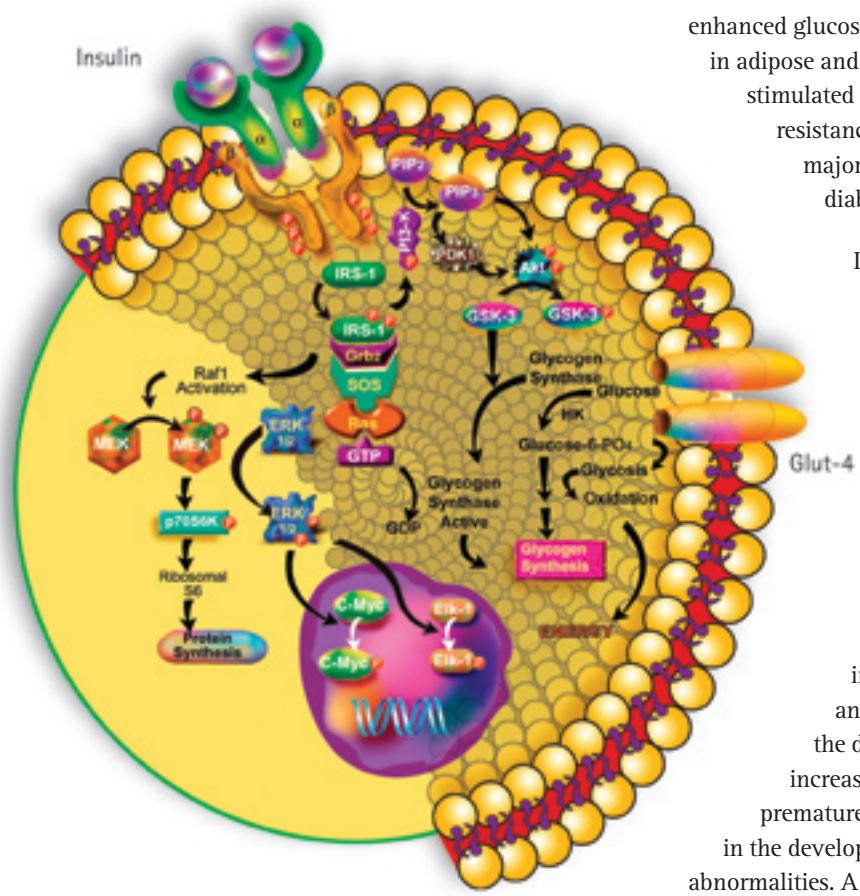
The Deadly Quartet of Metabolic Syndrome X

Chandra Mohan, Ph.D., EMD Chemicals, San Diego, CA 92121

Diabetes, a chronic metabolic disorder, affects about 5% of the population in the industrialized nations and accounts for over $200 billion in medical costs. In the year 2005, diabetes, directly and indirectly, accounted for about 3 million deaths worldwide. Type l diabetes often manifests in childhood and may result from autoimmune destruction of the 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.

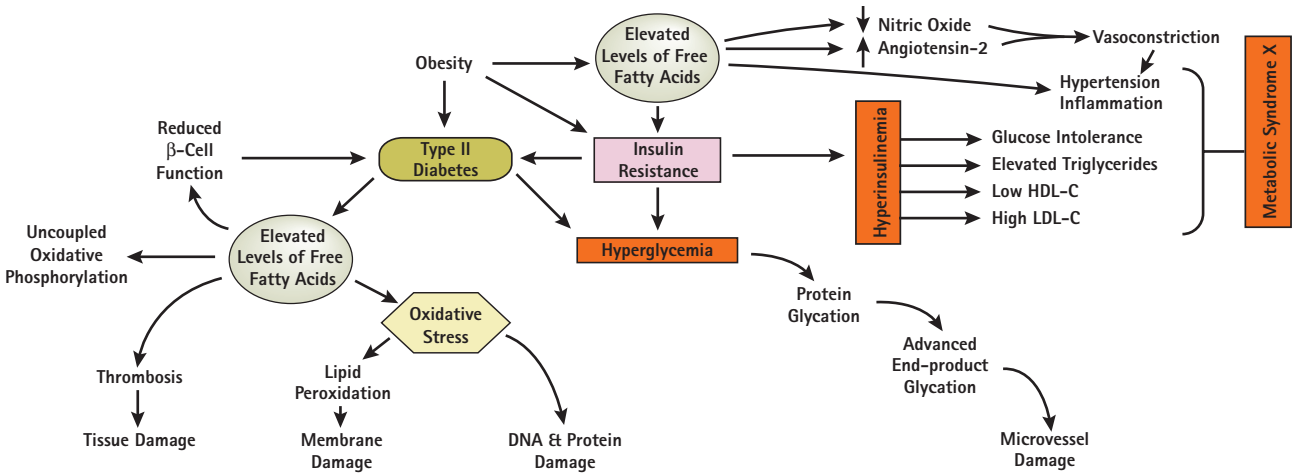
Insulin is the major hormone that counters the concerted action of a number of hyperglycemia-generating hormones. It enhances glucose uptake in muscle and adipose tissue, and reduces gluconeogenesis and lipolysis. Insulin resistance, caused by obesity, can result in elevated fasting and postprandial 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 trans-phosphorylates 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.

PI 3-K plays a critical role in the metabolic actions of insulin. Inhibitors of class 1a PI 3-K, such as LY 294002 block most metabolic actions of insulin, including stimulation of glucose transport, and glycogen and lipid synthesis. Activated PI 3-K phosphorylates PIP_2 to generate PIP_3, which then enlists 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} (for Akt1) or Thr^{309} and Ser^{474} (for Akt2) by PDK1 and mTORC2, respectively to achieve full activation. Akt phosphorylates GSK-3 and inactivates it, which then allows the activation of glycogen synthase to proceed. GSK-3 has been implicated in the multi-factorial etiology of skeletal muscle insulin resistance in obese animal models and in obese type II diabetics. Overexpression and hyperactivity of GSK-3 in skeletal muscle of obese type 2 diabetics has been linked with an impaired ability of insulin to activate glucose disposal and glycogen synthase. Selective inhibition of GSK-3 in insulin-resistant skeletal muscle tissue is shown to improve insulin-stimulated glucose transport.



In the overall scheme of glucose homeostasis in the body, skeletal muscle and adipose tissue are two major glucose-utilizing tissues in the absorptive state and glucose uptake by these tissues plays an important role in determining the glycemic state. Any alteration in insulin-stimulated glucose uptake can lead to derangements in whole body glucose disposal. In the unstimulated state, GLUT4 vesicles are sequestered inside cells, and their translocation is arrested. Activation of Akt is closely linked to the translocation of GLUT4 vesicles to the cell membrane where they participate in the transport of glucose. Although activation of PI 3-K is required for GLUT4 trafficking, it is considered to be inadequate to produce GLUT4 translocation. It has been suggested that the insulin-stimulated tyrosine phosphorylation of Cbl is an essential co-event. Cbl is recruited to the insulin receptor by the adapter protein CAP. Phosphorylated Cbl is translocated to lipid rafts. Blocking this step is shown to completely inhibit the stimulation of GLUT4 translocation by insulin. Phosphorylated Cbl recruits the CrkII-C3G complex to lipid rafts, where C3G activates TC10, a small GTP-binding protein. The activation of TC10 is shown to be essential for insulin-stimulated glucose uptake and GLUT4 translocation. The TC10 pathway functions in parallel with PI 3-K to fully stimulate GLUT4 translocation in response to insulin. Elevated cell surface levels of the GLUT4 facilitate enhanced glucose uptake from the circulation and storage in adipose and muscle tissue. Hence, defects in insulin-stimulated GLUT4 translocation are important in insulin resistance; and consequently GLUT4 has become a major pharmacological target for the treatment of diabetes mellitus and insulin resistance.

In addition to an impairment in insulin-stimulated recruitment of GLUT4 transporter from its intracellular storage compartment to the cell surface, insulin resistance observed in obesity and type II diabetes is characterized by many other defects, including decreases in the number of insulin receptors and their tyrosine kinase activity, the concentration and phosphorylation of IRS-1 and -2, and PI 3-K activity. These abnormalities result in a variety of metabolic defects, including hyperglycemia, hyperlipidemia, and hyperinsulinemia, which contribute to the development of metabolic syndrome X and increase the risk of cardovascular disorders and premature death. 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 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 FFAs 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 J_2, 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 diabetes subjects who exhibit metabolic syndrome X, which is characterized by clustering of atherosclerotic cardiovascular disease risk factors, including insulin resistance, obesity, hypertension, and dyslipidemia/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 vasodilation. 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 as a major etiologic mechanism. 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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Akt/PKB Signaling

Akt (protein kinase B), a serine/threonine kinase, is a critical enzyme in several signal transduction pathways involved in cell proliferation, apoptosis, angiogenesis, and diabetes. In mammals three isoforms of Akt have been reported (α, β, γ or Akt 1, 2, 3) that exhibit a high degree of homology, but differ slightly in the localization of their regulatory phosphorylation sites. Akt1 plays an important role in growth and anti-apoptosis; Akt2 acts primarily as a regulator of glucose metabolism. Although Akt3 does not contribute significantly to the maintenance of normal metabolism in tissues, it is essential for the attainment of normal organ size, probably influencing both cell size and number via mTOR activation. Activation of Akt involves growth factor binding to a receptor tyrosine kinase and activation of PI 3-K that phosphorylates membrane bound PIP_2 to generate PIP_3. The binding of PIP_3 to the PH domain anchors Akt to the plasma membrane. Akt is activated following its phosphorylation at Thr^{308} on the kinase domain by PDK1 and on Ser^{473} on the hydrophobic motif by PDK2.

The principal role of Akt in the cell is to facilitate growth factor-mediated cell survival and to block apoptotic cell death. Akt achieves this by phosphorylating a variety of substrates, such as Bad, caspase-9, Forkhead transcription factors, and GSK-3. Insulin receptors in all insulin-sensitive tissues are coupled to Akt, which phosphorylates and inactivates GSK-3. The activity of GSK-3 is inhibited by N-terminal serine phosphorylation of the two GSK-3 isoforms, Ser^{9} in GSK-3β and Ser^{21} in GSK-3α. Hence, insulin increases the phosphorylation of both Akt and GSK-3. In adipose tissue and skeletal muscle these kinases are usually in their dephosphorylated state induced by insulin resistance and diabetes.

Most commercially available Akt inhibitors do not compete for the ATP-binding site. They act by either preventing the generation of PIP_3 by PI 3-K or by blocking the binding of PIP_3 to Akt. This inhibitory mode is utilized by the PIP_3 analogs (Cat. No. 124005, 124008, 124009) and by a peptide derived from the proto-oncogene TCL1, which binds to the same region on the PH domain as PIP_3 (Cat. No. 124013 and 124014). Another mode of inhibition is by preventing the activation of Akt via inhibition of upstream affectors. Akt Inhibitor IV (Cat. No. 124011) and Akt Inhibitor V, Triciribine (Cat. No. 124012) belong to this category of inhibitors. Akt Inhibitor IV is an ATP-competitive inhibitor of a kinase upstream of Akt, but downstream of PI 3-K whereas Akt Inhibitor V, Triciribine targets an Akt effector molecule other than PI 3-K or PDK1.

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Antibodies

Product	Cat. No.	Comments	Size	Price
Anti-Akt, PH Domain Mouse mAb (SKB1)	ST1088	Monoclonal IgG, purified. Immunogen: a recombinant protein consisting of amino acids 1-149 of human Akt 1 fused to GST. Recognizes the ~60 kDa Akt protein in A431 cells. Reacts with human, rat. **FC, IB, IP**	1 set	
Anti-Akt1 (88-100) Rabbit pAb	530311	Polyclonal IgG, purified. Immunogen: a synthetic peptide corresponding to amino acids 88-100 of the human Akt1, conjugated to KLH. Reacts with human, mouse, rat, *Xenopus*. **ELISA, IB, IP**	100 µg	
PhosphoDetect™ Anti-Akt1 (pSer^{473}) Mouse mAb (11E6)	124003	Monoclonal IgG, purified. Immunogen: a synthetic phosphopeptide corresponding to amino acids surrounding the Ser^{473} phosphorylation site of human Akt1. Reacts with human, mouse. **ELISA, IB**	1 set	
PhosphoDetect™ Anti-Akt1 (pThr^{308}) Rabbit pAb	124001	Polyclonal IgG, purified. Immunogen: a synthetic phosphopeptide corresponding to amino acids surrounding the Thr^{308} phosphorylation site of human Akt1. Reacts with human, mouse. **IB**	10 T	
Anti-Akt2 Rabbit pAb	124002	Polyclonal IgG, undiluted serum. Immunogen: a synthetic peptide corresponding to a 16-amino acid sequence at the C-terminus of rat Akt2, conjugated to KLH. Reacts with human, mouse, rat. **ELISA, IB**	100 µl	
Anti-Akt1 (Ab-1) (135-145) Rabbit pAb	PC510	Liquid, undiluted serum. Recognizes the ~60 kDa Akt1 protein in NIH/3TC cells. Reacts with human, mouse. **IC**	50 µl	
Anti-PDK1 (1-556) Rabbit pAb	ST1115	Polyclonal IgG, undiluted serum. Immunogen: full length recombinant human PDK1. Recognizes ~60 kDa PDK1 in HEK293 cells. Also recognizes in 400 kDa and ~17 kDa unidentified proteins. **IB**	50 µl	

ELISA: enzyme-linked immunosorbent assay; **FC**: flow cytometry; **IB**: immunoblotting; **IC**: immunocytochemistry; **IP**: immunoprecipitation; **mAb**: monoclonal; **pAb**: polyclonal

Akt Activity Assay Kits

Akt Activity Immunoassay Kit

Format: Immunoblot
Assay time: 4 h
Sample type: Cell lysates, tissue extracts

A non-radioactive assay kit for measuring Akt activity in cell lysates or tissue extracts from human, mouse, and rat. Akt is first enriched via immunoprecipitation with an anti-Akt antibody and then tested for its ability to phosphorylate GSK-3α, an Akt substrate. Phosphorylated GSK-3α is detected through immunoblotting with anti-GSK-3α phospho-specific antibody.

Cat. No. 124007 **1 kit**

PhosphoDetect™ Akt (pSer^{473}) ELISA Kit

Format: 96-well plate
Sensitivity: ≤0.8 units/ml
Assay time: 4 h
Sample type: Cell lysates

A solid-phase sandwich ELISA kit that employs a monoclonal antibody specific for Akt (regardless of phosphorylation state) coated onto the wells of a 96-well plate. This kit is designed to detect and quantify the level of Akt protein that is phosphorylated at Ser^{473}. Although designed for use with human cell lines, is also suitable for use with mouse and rat cells.

Cat. No. CBA005 **1 kit**

PhosphoDetect™ Akt (pThr^{308}) ELISA Kit

Format: 96-well plate
Sensitivity: ≤0.8 units/ml
Assay time: 4 h
Sample type: Cell lysates

A solid-phase sandwich ELISA kit that employs a monclonal antibody specific for Akt (regardless of phosphorylation state) coated onto the wells of a 96-well plate. Detects Akt phosphorylated on Thr^{308}. The sensitivity of this ELISA was compared to Western blotting using known quantities of Akt (pThr^{308}). Although this kit was developed for human samples, it has also been found to be suitable for use with mouse and rat.

Cat. No. CBA004 **1 kit**

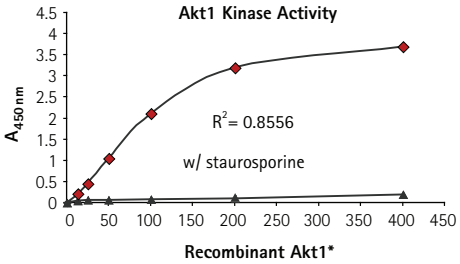
Akt/PKB Signaling

Akt Activity Assay Kits *(continued)*

K-LISA™ Akt Activity Kit

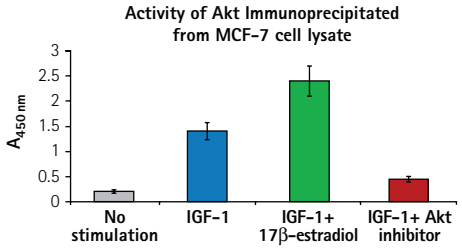
Format: 96-well plate
Sensitivity: 0.05 mU
Assay time: 3 h
Sample type: Cell lysates, tissue extracts, and purified enzyme

This 96-well ELISA-based kit is designed for the colorimetric detection of Akt activity in purified or partially purified preparations and for *in vitro* Akt inhibitor screening. The kit utilizes an N-terminal biotinylated peptide substrate (GRPRTSSFAEG) that is phosphorylated on the second serine by Akt1, Akt2, Akt3, SGK, and MSK1. *Sold under license of U.S. Patent 6,441,140.*



* 580 Units/mg; 1 Unit is equal to 1 nmol phosphate incorporated in substrate per min at 30°C

Activity of purified Akt in the presence and absence of Staurosporine (Cat. No. 569396). The activity of recombinant human Akt1 (Cat. No. 124006) (15-400 ng) was determined using the K-LISA™ Akt Activity Kit. Final concentration of Staurosporine was 1 µM. Assay range: 10-200 ng (580 units/mg).



Near-confluent MCF-7 cells were stimulated with IGF-1 (100 ng/ml) or IGF-1 (100 ng/ml) and 17β-estradiol (Cat. No. 3301) (500 nM) for 30 min at 37°C. For inhibition of Akt, cells were pre-incubated at 37°C for 15 min in the presence of Akt Inhibitor II (Cat. No. 124008) followed by stimulation with IGF-1 (100 ng/ml) for 30 min at 37°C. Cell lysates were prepared using PhosphoSafe™ Extraction Reagent (Cat. No. 71296-3). Equal amounts of total protein (1.5 mg) were immunoprecipitated and activity was determined.

Cat. No. CBA019 **1 kit**

TruLight™ Akt1/PKBα Kinase Assay Kit

Sensitivity: 25 pM
Assay time: 2 h
Sample type: recombinant or purified enzyme

A 96-well, sensitive, and high-speed homogenous assay for detection of Akt activity and for screening of Akt1/PKBα inhibitors in a high-throughput screening format. This kit is based on a fluorescence superquenching technology that does not require antibodies or radioactive labeling.

Cat. No. 539705 **1 kit**

Akt Inhibitors

Product	Cat. No.	Comments	Size	Price
Akt Inhibitor	124005	A phosphatidylinositol ether analog that potently and selectively inhibits Akt (IC_{50} = 5.0 µM). A weak inhibitor of phosphatidylinositol 3-kinase (IC_{50} = 83 µM). *Purity:≥95% by TLC.* M.W. 578.8	1 mg	
Akt Inhibitor II (SH-5)	124008	A phosphatidylinositol analog that inhibits the activation of Akt and selected downstream substrates without affecting the phosphorylation of PDK-1 and other downstream kinases. Decreases phosphorylation of Akt without affecting the total Akt level. *Purity:≥98% by NMR.* M.W. 598.7	1 mg	
Akt Inhibitor III (SH-6)	124009	A phosphatidylinositol analog that inhibits the activation of Akt and selected downstream substrates without affecting the phosphorylation of PDK-1 and other downstream kinases. Decreases phosphorylation of Akt without affecting the total Akt level. *Purity:≥98% by NMR.* M.W. 568.7	1 mg	
Akt Inhibitor IV	124011	A cell-permeable inhibitor of Akt phosphorylation/activation that targets ATP-binding site of a kinase upstream of Akt, but downstream of PI 3-Kinase. *Purity:≥98% by HPLC.* M.W. 614.6	1 mg 5 mg	

Akt Inhibitors *(continued)*

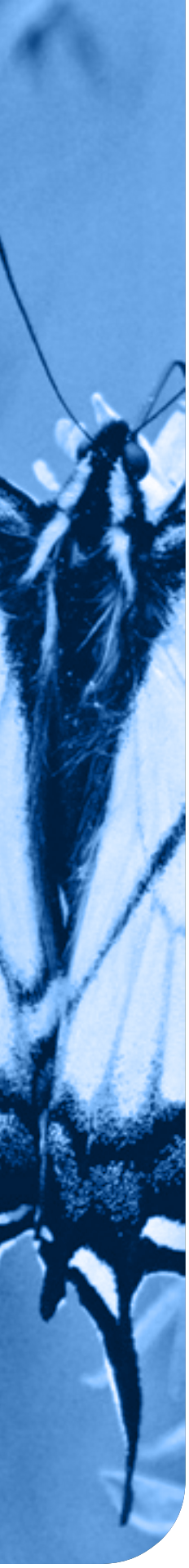
Product	Cat. No.	Comments	Size	Price
Akt Inhibitor IX, API-59CJ-OMe	124019	A cell-permeable ellipticine compound that potently and selectively inhibits cell growth and induces apoptosis in human endometrial cancer cells with elevated Akt levels. (Effective concentration: 12-24 µM). Exhibits minimal effect on cells lacking Akt activity. *Purity:≥95% by HPLC.* M.W. 404.5	5 mg	
Akt Inhibitor V, Triciribine	124012	A cell-permeable inhibitor of the cellular phosphorylation/activation of Akt 1/2/3 that targets an Akt effector molecule other than PI 3-K or PDK1. *Purity:≥95% by HPLC.* M.W. 320.3	1 mg	
Akt Inhibitor VI, *Akt-in*	124013	A 15-mer peptide that acts as a specific inhibitor of Akt. Shown to bind to Akt-PH domain (K_d ~18 µM) and interfere with the Akt-phosphoinositide interaction. *Purity:≥95% by HPLC.* M.W. 1871.1	2 mg	
Akt Inhibitor VII, TAT-*Akt-in*	124014	A cell-permeable version of the Akt Inhibitor VI, *Akt-in* (Cat. No. 124013) that directly binds Akt PH domain, preventing PI binding. *Purity:≥95% by HPLC.* M.W. 3412.9	2 mg	
Akt Inhibitor VIII, Isozyme-Selective, Akti-1/2	124018	A cell-permeable potent and selective inhibitor of Akt1/Akt2 kinase activity (IC_{50} = 58 nM, 210 nM, and 2.12 µM for Akt1, Akt2, and Akt3, respectively, in *in vitro* kinase assays). The inhibition is PH domain dependent. *Purity:≥95% by HPLC.* M.W. 551.6	1 mg	
InSolution™ Akt Inhibitor VIII, Isozyme-Selective, Akti-1/2	124017	A 10 mM (1 mg/181 µl) solution of Akt Inhibitor VIII, Isozyme-Selective, Akti-1/2 (Cat. No. 124018 in DMSO. *Purity:≥95% by HPLC.* M.W. 551.6	1 mg	
Akt Inhibitor X	124020	A cell-permeable, selective inhibitor of the phosphorylation of Akt and its *in vitro* kinase activity (complete inhibition < 5 µM) with minimal effect on PI 3-K, PDK1, or SGK1. Unlike Akti1/2 (Cat. No. 124018), the mode of inhibition is not PH domain-dependent. *Purity:≥95% by HPLC.* M.W. 381.4	5 mg	
Akt Inhibitor XI	124028	A cell-permeable copper complex (Cu^{2+}/Cu^{+} redox couple in the range of +0.28 to +0.35 V) that interacts with both the PH and the kinase domains of Akt and potently inhibits its kinase activity (IC_{50} = 100 nM). *Purity:≥98% by Elemental Analysis.* M.W. 381.7	5 mg	
PDK1/Akt/Flt Dual Pathway Inhibitor	521275	A cell-permeable inhibitor of both PDK1 and Akt activities in *in vitro* kinase assays. Blocks cellular phosphorylation of Akt at both Ser^{473} and Thr^{308}. *Purity:≥98% by HPLC (sum of 2 isomers).* M.W. 224.2	5 mg	

Proteins/Enzymes

Product	Cat. No.	Comments	Size	Price
Akt1, His•Tag®, Activated, Human, Recombinant, *S. frugiperda*	124006	Purified recombinant human Akt1 expressed in Sf9 cells. Highly active form of Akt1 suitable for phosphorylation of Akt substrates. Features a polyhistidine tag to facilitate removal of the enzyme from the reaction mixture. *Specific activity:≥20,000 units/mg protein. Purity:≥95% by SDS-PAGE.* M.W. 60,000	20 µg	
Akt2, GST-Fusion Protein, Active, Human, Recombinant, Insect Cells	124021	Human, recombinant Akt2 consisting of amino acids 1-119 (minus the PH domain) expressed as a GST fusion protein (N-terminal) using a baculovirus expression system. The recombinant protein is also expressed with S473D and T308E mutations. *Specific activity:≥ 45 units/µg. Purity: >80% by SDS-PAGE.* M.W. 68,000	20 µg	
Akt3, GST-Fusion Protein, Active, Human, Recombinant, *S. frugiperda*	124022	Full-length, human, recombinant Akt3 fused to GST at the N-terminus and expressed Sf9 cells using a baculovirus expression system. *Specific activity:≥ 176 nmol/min/mg protein. Purity: >92% by SDS-PAGE.* M.W. 84,000	5 µg	
PDK1, His•Tag®, Human, Recombinant, *S. frugiperda*	521270	Full length PDK1 expressed in insect cells. PDK1 is a Serine/Threonine protein kinase that is localized to the plasma membrane. *Specific activity:≥80 units/mg protein. Purity:≥90% by SDS-PAGE.* M.W. 66,867	5 µg	

Akt Substrates

Product	Cat. No.	Comments	Size	Price
AKTide-2T	123900	An optimal peptide substrate for assaying Akt/PKB/Rac-protein kinase activity *in vitro*. The peptide undergoes phosphorylation at the Ser site (K_m = 3.9 µM). Competitively inhibits histone H2B phosphorylation (K_i = 12 µM) by Akt. *Purity:≥95% by HPLC.* M.W. 1715.9	1 mg	
Crosstide	233612	A peptide analog of GSK-3 that functions as a natural substrate for Akt in the presence of ATP. Displays similar specificities towards PKBα, PKBβ and PKBγ isoforms (K_m = 4 µM). *Purity: >97% by HPLC.* M.W. 1164.2	1 mg	
Protein Kinase Bα Substrate	539622	A specific substrate for Protein Kinase B_α (K_m = 5 µM). *Purity: >98% by HPLC.* M.W. 817	1 mg	



Phosphoinositide 3-Kinases (PI 3-K)

The PI 3-kinases are ubiquitous, heterodimeric lipid kinases that play a pivotal role in the regulation of many cellular processes, including cell growth, motility, proliferation, and survival. They are dual-specificity enzymes capable of phosphorylating phosphoinositides. The PI 3-kinase family has eight members divided into four major classes that differ in their substrate selectivity and regulation. Class IA kinases were the first to be characterized and include receptor-regulated heterodimeric enzymes consisting of a 110 kDa catalytic subunit (α, β, δ) and a regulatory subunit (p85α, p85β, p55α, p50α). They can use PI, PI (4)P and PI (4,5)P_2, as substrates *in vitro*. The major substrate *in vivo* appears to be PI(4,5)P_2, which generates PI(3,4,5)P_3. The members of this class are sensitive to wortmannin. Class IB has only one member with a p110γ catalytic subunit and a p101 regulatory subunit. Class II members (PI 3-K C2α, PI 3-K C2β, PI 3-K C2γ) are associated with membrane structure and can phosphorylate PI and PI(4)P *in vitro* and show variable responses to wortmannin. This class of enzymes contains a C-2 domain at the C-terminal region that binds phospholipids in a Ca^{2+}-dependent manner. They participate in integrin signaling in platelets. Class III PI 3-kinases includes Vps34 that can phosphorylate PI(3)P. The human homologue of Vps34 is reported to be sensitive to wortmannin and participates in the regulation of endocytic membrane trafficking.

Activated PI 3-kinase phosphorylates phosphoinositol (PI) substrates to produce PI(3)P, PI(3,4)P_2, and PI(3,4,5)P_3. These molecules act as second messengers and recruit the PI 3-K-dependent serine/threonine kinases (PDK1) and Akt from the cytoplasm to the plasma membrane. Lipid binding and membrane translocation lead to conformational changes in Akt, which gets phosphorylated on Thr^{308} in the activation loop, and Ser^{473} in the hydrophobic phosphorylation motif by PDK1. This dual phosphorylation causes full activation of the enzyme. Inhibitors of PI 3-kinase and over-expression of dominant negative PI 3-kinase mutants are shown to block many of the physiological responses of a cell to insulin, indicating that PI 3-kinase lies upstream of these events.

Dysregulated PI 3-K signaling pathway has been reported in a variety of human tumors. Over 30% of various solid tumors are reported to contain mutations in the catalytic unit of their PI 3-K. Functional analyses of the catalytic subunit of PI 3-K mutations indicate that these mutations abnormally increase its enzymatic activity, stimulate AKT signaling, allow growth factor-independent growth as well as increasing cell invasion and metastasis. Hence, PI 3-kinase is becoming an attractive target for drug development, not only in the areas of cancer and other proliferative diseases, but also in the treatment of diabetes, inflammation, and immunological conditions.

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Stein, R.C, and Waterfield, M.D. 2000. *Mol. Med. Today* **6,** 347.
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Antibodies

Product	Cat. No.	Comments	Size	Price
Anti-PI-3-Kinase Mouse mAb (AB6)	528107	Monoclonal IgG, purified. Immunogen: recombinant human p85α expressed in *E. coli*. Recognizes p85α subunit of PI 3-Kinase. Reacts with human, mouse, rat. **IB, IC, IP**	100 µg	
Anti-PI-3-Kinase p110δ, C-Terminal (1026-1044) Rabbit pAb	526553	Polyclonal IgG, purified. Immunogen: a synthetic peptide [(C)SWKTKVNWLAHNVSKDNRQ) corresponding to a distinct C-terminal region of human phosphatidylinositol 3-kinase p110δ, conjugated to KLH. Reacts with human. **IB, IC**	100 µl	

IB: immunoblotting; **IC**: immunocytochemistry; **IP**: immunoprecipitation; **mAb:** monoclonal **pAb**: polyclonal

Kit

TruLight™ Phosphoinositide 3-Kinase Assay Kit

Format: 384-well plate
Detection method: Fluorescence
Assay time: 2 h
Sample type: Purified enzyme

A sensitive and high-speed homogeneous assay for the detection of PI 3-K activity and for screening of PI 3-K inhibitors in a high-throughput screening format. This kit is based on a fluorescence superquenching technology that does not require antibodies or radioactive label.

Cat. No. 539718 **1 kit**

PI 3-Kinase Inhibitors

Product	Cat. No.	Comments	Size	Price
PI-103	528100	A cell-permeable, potent, and ATP-competitive inhibitor of DNA-PK, PI 3-K, and mTOR (IC_{50} = 2, 8, 88, 48, 150, 26, 20, and 83 nM for DNA-PK, p110α, p110β, p110δ, p110γ, PI3-KC2β, mTORC1, and mTORC2, respectively). *Purity:≥97% by HPLC.* M.W. 348.4	1 mg 5 mg	
PI 3-Kγ/CKII Inhibitor	528112	A cell-permeable, potent, ATP-competitive, dual-specific inhibitor of PI 3-K/CKII (IC_{50} = 20 nM) with selectivity over PI 3-Kα, β, and δ (IC_{50} = 940 nM, 20 µM, and 20 µM, respectively). *Purity:≥98% by HPLC.* M.W. 305.3	5 mg	
PI 3-Kγ Inhibitor	528106	A cell-permeable, 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	5 mg	
PI 3-Kγ Inhibitor II	528108	A cell-permeable, potent, and ATP-competitive inhibitor of PI 3-Kγ (K_i = 180 nM; IC_{50} = 250 nM). Exhibits great selectivity over PI 3-Kα (IC_{50} = 4.5 µM), PI 3-Kβ and δ (IC_{50} > 20 µM). *Purity:≥98% by HPLC.* M.W. 285.2	5 mg	
PI 3-Kα Inhibitor IV	528111	A cell-permeable, potent, and isoform-selective inhibitor of PI 3-Ks (IC_{50} = 2 nM, 16 nM, 660 nM, and 220 nM for p110α, p110β p110γ, and PI 3-K C2β respectively) and inhibits non-PI 3-K kinases only at much higher concentrations (IC_{50} ≥3.4 µM for Cdk2/E, KDR, PKA, and PKCα). *Purity:≥95% by HPLC.* M.W. 386.3	5 mg	
LY 294002	440202	A cell-permeable, potent and specific inhibitor of PI 3-kinase that acts on the ATP binding site of the enzyme (IC_{50} = 1.4 µM). *Purity:≥98% by HPLC.* M.W. 307.4	5 mg	
InSolution™ LY 294002	440204	A 10 mM (1 mg/325 µl) solution of LY 294002 (Cat. No. 440202) in anhydrous DMSO.	1 mg	
LY 303511	440203	A negative control for the PI 3-kinase inhibitor, LY 294002 (Cat. No. 440202). Contains a single atom substitution in the morpholine ring compared to LY 294002. Does not affect PI 3-kinase activity even at concentrations ≥100 µM. *Purity:≥98% by HPLC.* M.W. 306.4	1 mg	
Quercetin, Dihydrate	551600	An inhibitor of PI 3-kinase (IC_{50} = 3.8 µM) and phospholipase A2 (IC_{50} = 2 µM). *Purity:≥98% by HPLC.* M.W. 338.3	100 mg	
Wortmannin	681675	A fungal metabolite that acts as a potent, selective, cell-permeable and irreversible inhibitor of PI 3-kinase in purifi ed preparations and cytosolic fractions (IC_{50} = 5 nM). Blocks the catalytic activity of PI 3-kinase without affecting the upstream signaling events. Also acts as an active site inhibitor that abolishes mTOR phosphorylation. *Purity:≥95% by HPLC.* M.W. 428.4	1 mg	

AMP-Activated Protein Kinase (AMPK)

5'-AMP-activated protein kinase (AMPK), a trimeric enzyme in mammals, consists of a catalytic α subunit (63 kDa) and the non-catalytic β and γ subunits. The N-terminus of the α subunit contains a serine/threonine kinase catalytic domain. The β and γ subunits interact with the C-terminal region of the α subunit. There are two genes that encode isoforms of both the α and β subunits (α1, α2, β1 and β2) and three genes encode isoforms of the γ subunit (γ1-γ3). The α2 isoform is found predominantly in skeletal and cardiac muscle. Hepatic tissue exhibits an equal distribution of both α1 and α2 isoforms, and in pancreatic β-cells largely the α1 isoform is expressed.

AMPK is activated by increases in the cellular AMP/ATP ratio caused by metabolic stress that either interferes with ATP production or accelerates ATP consumption. AMP affects AMPK by a direct allosteric activation thereby making it a poor substrate for dephosphorylation. Even a small increase in AMP levels can induce a significant increase in the activity of AMPK. AMPK is activated by phosphorylation at Thr^{172} in the activation loop by one or more upstream AMPK kinases, including Akt. LKB1, an upstream constitutively active protein kinase, phosphorylates AMPK when AMP levels are elevated in cells. In addition, Ca^{2+}/CaM kinase β is shown to phosphorylate and activate AMPK when calcium levels are increased, independent of any increase in AMP levels.

AMPK stimulates pathways that are linked to increased energy production, such as glucose transport and fatty acid oxidation. On the other hand, it switches off the energy consuming pathways, such as lipogenesis, protein synthesis, and gluconeogenesis.

References:

Towler, M.C., and Hardie, D.G. 2007. *Circ. Res.* **100,** 328.
Daval, M., et al. 2006. *J. Physiol.* **574,** 55.
Kahn, B.B., et al. 2004. *Cell Metab.* **1,** 15.
Rutter, G.A. et al. 2003. *Biochem. J.* **375,** 1.

Antibodies

Product	Cat. No.	Comments	Size	Price
Anti-AMPKα-2 Rabbit pAb	ST1089	Polyclonal IgG, purified. Immunogen: a synthetic peptide corresponding to a portion of mammalian AMP-activated protein kinase, α-2 (AMPKα-2) subunit encoded within exon 7 (LocusLink ID 5563). Recognizes ~64 kDa AMPKα-2 in aortic endothelial cells. Reacts with bovine, human, rat. **IB, IP**	50 µg	
Anti-LKB1 (120-160) Rabbit pAb	ST1092	Polyclonal IgG_1, immunoaffinity, purified. Immunogen: a synthetic peptide located between amino acid residues 120-160 of human LKB1. Detects 47 kDa LKB1 protein. Reacts with human. **IB**	50 µg	

IB: immunoblotting; **IP**: immunoprecipitation; **pAb**: polyclonal

AMP-Activated Protein Kinase (AMPK)

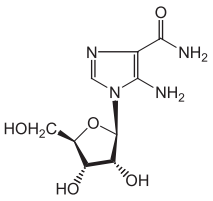
AMPK Inhibitors

Product	Cat. No.	Comments	Size	Price
AMPK Inhibitor, Compound C	171260	A cell-permeable, potent, selective, reversible, and ATP-competitive inhibitor of AMPK (AMP-activated protein kinase; K_i = 109 nM in the presence of 5 µM ATP and the absence of AMP). Blocks cellular activities induced by AICAr (Cat. No. 123040) or Metformin. Induces weight loss by attenuating AMPK-mediated food intake in mice. *Purity:≥95% by HPLC.* M.W. 399.5	1 mg 5 mg	
InSolution™ AMPK Inhibitor, Compound C	171261	A 10 mM (1 mg/250 µl) solution of AMPK inhibitor, compound C (Cat. No. 171260) in DMSO.	1 mg	
(-)-Deguelin, *Mundulea sericea*	252740	A cell-permeable inhibitor of mitochondrial bioenergetics (IC_{50} = 6.9 nM for NADH: ubiquinone oxidoreductase in bovine heart ETP). Reported to activate AMPK activity. *Purity:≥98% by HPLC.* M.W. 394.4	5 mg	
STO-609	570250	A cell-permeable, highly selective, potent, ATP-competitive inhibitor of CaM-kinase Kinase. Blocks TCR-mediated activation of AMPK activity. *Purity:≥95% by HPLC.* M.W. 374.4	5 mg	

AMPK Activators

AICA-Riboside

A cell-permeable nucleoside compound whose phosphorylated metabolite activates AMPK. 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**

AICA-Riboside, 5′-Phosphate

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

Cat. No. 123041 **25 mg**

AMPK Activator (D942)

A cell-permeable, indirect activator of AMPK that acts by inhibiting mitochondrial complex I. 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**

1,1-Dimethylbiguanide, Hydrochloride

An antihyperglycemic agent that lowers blood glucose levels without stimulating insulin secretion. Reported to stimulate AMPK leading to the reduction in acetyl-CoA carboxylase activity and induction of fatty acid oxidation. M.W. 165.6

Cat. No. 317240 **5 g**

Leptin, Human, Recombinant, *E. coli*

For more information, see page 54
(Leptins and Leptin Receptors)

Cat. No. 429700

Leptin, Mouse, Recombinant, *E. coli*

For more information, see page 54
(Leptins and Leptin Receptors)

Cat. No. 429705

mTOR: A Master Regulator of Growth Factor Signaling

The mammalian target of rapamycin (mTOR), a 298 kDa evolutionarily conserved serine/threonine kinase, acts as a nutrient sensor and regulates growth factor signaling and cellular metabolism. The catalytic kinase domain of mTOR, located in the in the C-terminal region, exhibits a strong homology to the catalytic domain of PI 3-K and PI 4-kinase. mTOR is considered as an important regulator of protein synthesis, translation initiation, transcription of ribosomal proteins, and the synthesis of rRNA and tRNA. mTOR is also shown to phosphorylate PP2A and block its activity. mTOR activates translation initiation in response to both hormonal and nutrient signals by phosphorylating p70S6 kinase 1 and eIF-4E-binding protein 1. Both mTOR and p70S6 kinase 1 are potently activated by insulin via the insulin receptor/IRS-1/PI 3-Kinase/Akt pathway signaling pathway. In this scheme of reactions Akt phosphorylates mTOR on Ser^{2448}.

mTOR and p70S6 kinase 1 activation by insulin is shown to be significantly higher in tissues of obese rats coupled with increased inhibitory phosphorylation at Ser^{636}/Ser^{639} on insulin receptor substrate-1 (IRS-1). Studies have shown that basal activation of mTOR and p70S6 kinase is higher in liver and skeletal muscle of obese rats fed a high fat diet, and this over-activated pathway may be involved in the development of insulin resistance in obese rats.

References:

Tsang, C-K., et al. 2007. *Drug Disc. Today* **12,** 112.
Tzatsos, A., and Kandror, K.V. 2006. *Mol. Cell Biol.* **26,** 63.
Khamzina, L., et al. 2005. *Endocrinology* **146,** 31473.
Asnaghi, L., et al. 2004. *Pharmacol. Res.* **50,** 545.
Patti, M.E., and Kahn, B.B. 2004. *Nat. Med.* **10,** 1049.
Tremblay, F., and Marette, A. 2001. *J. Biol. Chem.* **276,** 38052.

Antibodies

Product	Cat. No.	Comments	Size	Price
Anti-4EBP1/PHAS-I (101-118) Rabbit pAb	516676	Polyclonal IgG, purified. Immunogen: a synthetic peptide corresponding to amino acids 101-118 of human PHAS-I, conjugated to KLH. Recognizes ~19-25 kDa multiple phosphorylation states of native and recombinant PHAS-I. Reacts with human, mouse, rat. **GS, IB**	100 µg	
PhosphoDetect™ Anti-p70S6K(pThr^{389}) Rabbit pAb	PK1015	Polyclonal IgG, purified. Immunogen: a synthetic phosphopeptide corresponding to amino acids surrounding the Thr^{389} phosphorylation site of human p70S6K. Recognizes the ~60 kDa p70S6 kinase protein phosphorylated on Tyr^{389} in MCF7 cells. Reacts with human. **ELISA, IB**	50 µg	
Anti-p70S6 Kinase Rabbit pAb	ST1046	Polyclonal IgG, purified. Immunogen: a synthetic peptide corresponding to the C-terminus of p70S6 kinase. Recognizes the ~70 kDa p70S6 kinase protein in serum-starved rat L6 myoblasts. Reacts with human, mouse, rat. **IB**	100 µg	
Anti-Raptor Rabbit pAb	ST1048	Polyclonal IgG, purified. Immunogen: a synthetic peptide corresponding to amino acids encoded within exon 26 of human raptor. Recognizes the ~150 kDa raptor protein. Reacts with human, mouse, rat. **IB**	100 µg	
Anti-mTOR/FRAP (Ab-2) Mouse mAb (22C2)	OP97	Monoclonal IgG. Immunogen: a synthetic peptide corresponding to amino acids 230-240 of human mTOR. Reacts with human. **IB, IP**	100 µg	
PhosphoDetect™ Anti-mTOR (pSer^{2448}) Rabbit pAb	PS1020	Polyclonal IgG, Purified. Immunogen: a synthetic phosphopeptide corresponding to amino acids surrounding the Ser^{2448} phosphorylation site of human mTOR. Detects ~290 kDa mTOR protein phosphorylated on Ser^{2448} in EGF-treated HEK293 cells. Reacts with human. **IB**	50 µg	
Anti-TSC1 (Tuberous Sclerosis 1) Rabbit pAb	AP1032	Polyclonal IgG, Purified. Immunogen: a synthetic peptide corresponding to amino acids 1100-1164 of human TSC1. Detects the ~120 kDa tuberous sclerosis 1 protein (TSC1) or hamartin. Reacts with human, mouse. **IB, IP**	50 µg	
PhosphoDetect™ Anti-Tuberin/TSC2 (pThr^{1462}) Rabbit pAb	ST1084	Polyclonal IgG, purified. Immunogen: a synthetic peptide corresponding to amino acids surrounding the Thr^{1462} phosphorylation site of human Tuberin/TSC2. Recognizes the ~200 kDa tuberin/TSC2 protein phosphorylated at Thr^{1462}. Reacts with human, mouse. **IB**	50 µl	

ELISA: enzyme-linked immunosorbent assay; **GS**: gel shift; **IB**: immunoblotting; **IP**: immunoprecipitation; **mAb**: monoclonal; **pAb**: polyclonal

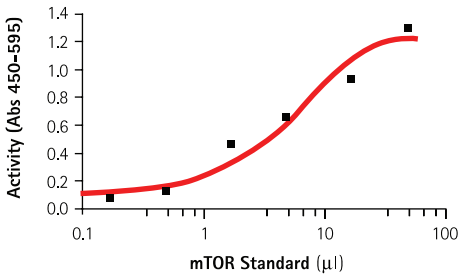
mTOR Related Kits

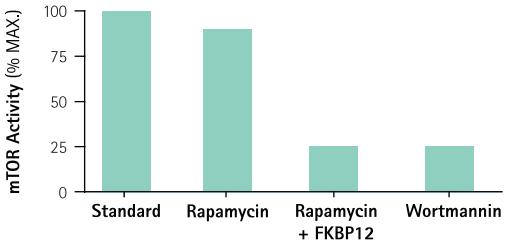
K-LISA™ mTOR Activity Kit

Format: 96-well plate

Sample type: Purified or partially purified enzyme

An ELISA-based activity assay for measuring the kinase activity of purified or mTOR immunoprecipitated from cell lysates. Useful for *in vitro* mTOR inhibitor screening and for assessing the regulation of mTOR cell signaling. This assay utilizes a p70S6K GST fusion protein as a specific mTOR substrate. *Sold under exclusive license of allowed U.S. patent application 20040191836.*





Activity of mTOR Standard

The mTOR Standard supplied in the kit is an enriched rat brain fraction isolated using proprietary methods. The mTOR standard phosphorylates p70S6K specifically on Thr^{389}, and is inhibited by FKBP12-rapamycin, a specific inhibitor of mTOR complex, as well as Wortmannin (Cat. No. 681675), a more general PI-3K inhibitor.

Inhibition of mTOR Standard kinase activity

Activity of the mTOR Standard was determined in the presence of either rapamycin (20 µM), GST-FKBP12 (37 mg/ml)/rapamycin (20 µM), a complex that specifically inhibits the mTOR/Raptor (regulatory associated protein of mTOR) complex, or Wortmannin (10 µM; included with the kit), a more general PI-3K inhibitor.

Cat. No. CBA055 **1 kit**

mTOR Signaling

mTOR Related Kits *(continued)*

TruLight™ p70S6 Kinase Assay Kit

Format: 96-well plate

Sample type: Recombinant or purified enzyme

A sensitive and high speed homogeneous assay for the detection of enzyme activity and for screening of p70S6 kinase inhibitors in a high-throughput screening (HTS) format. This kit is based on a fluorescence superquenching technology that does not require antibodies or radioactive label.

Cat. No. 539711 **1 kit**

mTOR Inhibitors

Product	Cat. No.	Comments	Size	Price
PI-103	528100	A cell-permeable, potent, and ATP-competitive inhibitor of DNA-PK, PI 3-K, and mTOR (IC_{50} = 2, 8, 88, 48, 150, 26, 20, and 83 nM for DNA-PK, p110α, p110β, p110δ, p110γ, PI3-KC2β, mTORC1, and mTORC2, respectively). *Purity:≥97% by HPLC.* M.W. 348.4	1 mg 5 mg	
Rapamycin	553210	Selectively inhibits the phosphorylation and activation of p70 S6 kinase (IC_{50} = 50 pM). Prevents the translational activation of IGF-II. Shown to inhibit later signaling events such as $p110^{Rb}$ phosphorylation, $p34^{cdk1}$ kinase activation, and cyclin A synthesis. *Purity:≥98% by HPLC.* M.W. 914.2	100 µg 1 mg	
Wortmannin	681675	A fungal metabolite that acts as a potent, selective, cell-permeable and irreversible inhibitor of PI 3-kinase in purified preparations and cytosolic fractions (IC_{50} = 5 nM). Blocks the catalytic activity of PI 3-kinase without affecting the upstream signaling events. Also acts as an active site inhibitor that abolishes mTOR phosphorylation. *Purity:≥95% by HPLC.* M.W. 428.4	1 mg	
InSolution™ Rapamycin	553211	A 5 mM solution of Rapamycin (Cat. No. 553210) in DMSO.	500 µg	

Proteins/Enzymes

p70S6K, Human, Recombinant, *S. frugiperda*

A full-length, active, recombinant, human p70 S6 kinase (p70S6K). *Activity: Kinase activity is measured as the amount of radioactivity incorporated into S6K substrate peptide (CKRRRLASLR) stat at 30˚C, using a final concentration of 50 mM [^{32}P] ATP. Purity: ≥75% by SDS-PAGE.* M.W. 76,000

Cat. No. 506182 **5 µg**

FKBP12, GST-Fusion, Human, Recombinant, *E. coli*

A Full-length recombinant, human FK506 binding protein 12-rapamycin associated protein 1 (FKBP12) fused to GST at the N-terminus and expressed in *E. coli*. FKBP12 is a cytosolic receptor for both rapamycin and FK506 that also serves as a natural cofactor for rapamycin's inhibition of mTOR. *Purity: ≥90% by SDS-PAGE.* M.W. 12,000

Cat. No. 325902 **60 µg**

Ref.: Jin, Y.J., et al. 1991. *Proc. Natl. Acad. Sci. USA* **88,** 6677.

Protein Tyrosine Phosphatases:

Their Role in Diabetes and Obesity

Insulin binding to the α-subunit of the insulin receptor stimulates the tyrosine kinase activity of the β-subunit, which results in phosphorylation of insulin-receptor substrates to propagate insulin signaling. Protein tyrosine phosphatases (PTP), particularly the protein tyrosine phosphatase-1B (PTP-1B), reduce the degree of phosphorylation of the insulin receptor, which diminishes insulin signaling and insulin sensitivity. A negative regulatory role for protein tyrosine phosphatases in insulin signaling and in the development of insulin resistance associated with Type 2 diabetes has been well established.

PTP-1B, a 37 kDa enzyme, is one of the most-studied non-receptor PTPs. It consists of a single domain organized into 8 α-helices and 12 β-sheets. Situated on loop 15, which connects β-12 and α-4, is Cys^{215}, which is critical to the catalytic function of PTP-1B. The base of the catalytic site is formed by the residues His^{214} through Arg^{221}. A structural feature that is highly conserved in PTP-1B is the catalytic or PTP loop, which consists of 11 residues: (I/V)HCXAGXXR(S/T)G wherein Cys^{215} and Arg^{221} are critical for catalysis. Another highly conserved region is the recognition pocket, which plays a role in substrate recognition. Tyr^{46} and Val^{49} assist the substrate's insertion into the catalytic site. Ser^{216} of the PTP loop forms a hydrogen bond with the recognition loop, which stabilizes the active site cleft. When a phosphorylated tyrosine residue comes in contact with the active site cleft, Tyr^{46} and Val^{49} of the recognition loop facilitate its entry into the site.

PTP-1B is considered as a negative regulator of insulin signaling and several genetic studies have supported the association between PTP-1B and insulin resistance. Mice lacking PTP-1B exhibit enhanced insulin sensitivity and even when fed a high fat diet maintain their insulin sensitivity. They are resistant to diabetes and diet-induced obesity. Hence, PTP-1B is considered as an effective target for the treatment of both Type 2 diabetes and obesity. A variety of vanadium compounds have been known to mimic the effects of insulin by inhibition of tyrosine phosphatases.

References:

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Pei, Z., et al. 2004. *Curr. Pharm. Res.***10,** 3481.
Goldstein, B.J. 2002. *J. Clin. Endocrinol. Metab.* **87,** 2474.
Kennedy, B.P., and Ramachandran, C. 2000. *Biochem. Pharmacol.* **60,** 877.
Ahmad, F., and Goldstein, B.J. 1995. *Am. J. Physiol. Endocrinol. Metab.* **268,** E932.

Protein Tyrosine Phosphatase-1B

PTP-1B and Related Antibodies

Product	Cat. No.	Comments	Size	Price
Anti-PTPase 1B (Ab-1) Mouse mAb (FG6-1G)	PH01	Monoclonal IgG_{2a}, purified. Immunogen: recombinant human protein tyrosine phosphatase 1B (PTPase 1B). Reacts with avian, hamster, human, mouse (weakly), rat. **IB, IF, IP**	100 µg	
Anti-PTPase 1B (Ab-2) Mouse mAb (AE4-2J)	PH02	Monoclonal IgG_1, purified. Immunogen: recombinant human protein tyrosine phosphatase 1B (PTPase 1B). Reacts with human. **IB, IF, IP**	100 µg	
PhosphoDetect™ Anti-PTEN ($pSer^{380}$) Rabbit pAb	ST1072	Polyclonal IgG, purified. Immunogen: a synthetic phosphopeptide corresponding to amino acids surrounding the Ser^{380} phosphorylation site of human PTEN. Recognizes the ~54 kDa PTEN protein phosphorylated at Ser^{380}. Reacts with human, mouse, rat. **IB, IC, IP, PS**	50 µl	
Anti-PTEN Mouse mAb (EMD-15E10)	AP1041	Monoclonal IgG_1, purified. Immunogen: recombinant full-length human PTEN expressed in Sf9 cells. Recognizes the ~55 kDa PTEN protein in MCF-7 cells. Reacts with human. **ELISA, IP**	50 µg	
Anti-PTEN Mouse mAb (EMD-4B8)	AP1042	Monoclonal IgG_1, purified. Immunogen: recombinant full-length human PTEN expressed in Sf9 cells. Recognizes the ~55 kDa PTEN protein in MCF-7 cells. Reacts with human. **IB**	50 µg	
Anti-SHP-1 Mouse mAb (1SH01)	566806	Monoclonal IgG_{2b}. Immunogen: recombinant human SHP-1. Recognizes the ~50 kDa SHP-1 protein in hematopoietic cells. Does not cross-react with other tyrosine phosphatases. **IB**	100 µg	
Anti-SHP-2 Rabbit pAb	ST1083	Polyclonal IgG, purified. Immunogen: a synthetic peptide corresponding to amino acids from the N-terminal domain of human SHP-2. Recognizes the ~72 kDa SHP-2 protein. SHP-2 plays a critical role in leptin signaling. Reacts with human, mouse, rat. **IB, IP, PS**	50 µl	
PhosphoDetect™ Anti-SHP-2 ($pTry^{542}$) Rabbit pAb	ST1082	Polyclonal IgG, purified. Immunogen: a synthetic peptide corresponding to amino acids surrounding the Tyr^{542} phosphorylation site of human SHP-2. Recognizes the ~72 kDa SHP-2 protein phosphorylated at Tyr^{542}. Reacts with human, mouse, rat. **IB, IP**	50 µl	

ELISA: enzyme-linked immunosorbent assay; **IB**: immunoblotting; **IC**: immunocytochemistry; **IF**: immunofluorescence; **IP**: immunoprecipitation; **PS**: paraffin sections; **mAb**: monoclonal; **pAb**: polyclonal

Protein Tyrosine Phosphatase Assay Kits

Protein Tyrosine Phosphatase 1B Assay Kit, Colorimetric

Format: 96-well format
Assay time: 2 h
Sample type: Purified enzyme

A colorimetric assay kit to measure PTP1B activity. This convenient 96-well assay is useful for screening inhibitors and modulators of PTP1B activity.

Cat. No. 539736 **1 kit**

Protein Tyrosine Phosphatase Assay Kit, Fluorometric

Format: 96-well format
Sensitivity: 0.2-0.4 pmol
Assay time: 2 h
Sample type: Purified enzyme

A fluorometric assay kit for the measurement of Protein Tyrosine Phosphatase (PTP) activity. The assay uses a fluorogenic phosphopeptide substrate quenched internally by resonance energy transfer. The substrate contains a fluorophore (MCA) and a quencher group (DNP) as well as a phosphotyrosine residue located between these groups. Reaction of the substrate with PTP followed by treatment of the dephosphorylated substrate with chymotrypsin results in the cleavage of the peptide, which results in an increase in fluorescence

Cat. No. 539742 **1 kit**

Protein Tyrosine Phosphatase-1B

Proteins/Enzymes

Product	Cat. No.	Comments	Size	Price
Protein Tyrosine Phosphatase 1B, Human, Recombinant, *E. coli*	539735	A ubiquitous prototype nontransmembrane protein tyrosine phosphatase. This highly active enzyme preparation is useful for the study of tyrosine phosphatase kinetics, substrate specificity, and for screening inhibitors. *Specific activity:≥ 20 units/mg. Purity: >95% by SDS-PAGE.* M.W. 37,400	50 µg	
Protein Tyrosine Phosphatase LAR, Human, Recombinant, *E. coli*	539731	Soluble catalytic domain (350 amino acids) of the human transmembrane leukocyte antigen-related protein tyrosine phosphatase. Involved in the modulation of insulin receptor signaling in intact cells. Suitable for dephosphorylation of phosphotyrosine residues in proteins. Inhibited by vanadate. *Specific activity:≥5000 units/mg protein. Purity: ≥95% by SDS-PAGE.* M.W. 40,000	200 U	
Protein Tyrosine Phophatase SHP-2, GST-Fusion, Human, Recombinant, *E. coli*	565855	The catalytic domain of human SHP-2 (amino acids 224-529) fused to an N-terminal GST. *Specific activity:≥2U/µg.* M.W. 59,000	20 µg	
PTEN, His•Tag® and S•Tag™, Human Recombinant, *S. frugiperda*	481409	Human full-length PTEN (**p**hosphatase and **ten**sin 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 U/mg protein. Purity: >80% by SDS-PAGE.* M.W. 53,000	10 µg	

Protein Tyrosine Phosphatase Substrates

Product	Cat. No.	Comments	Size	Price
Protein Tyrosine Phosphatase 1B Substrate I (DADEpYLIPQQG)	539737	Substrate for mammalian Protein Tyrosine Phosphatase 1B (Cat. No. 539735; K_m = 3.9 mM) and *Yersinia* Protein Tyrosine Phosphatase (Cat. No. 539734). The sequence is derived from an autophosphorylation site (Tyr^{992}) of EGFR. The assay is based on marked differences in the spectra of peptide before and after the removal of the phosphate group. *Purity:≥97% by HPLC.* M.W. 1330.3	1 mg	
Protein Tyrosine Phosphatase 1B Substrate II (Ac-ELEFpYMDYE-NH_2)	539739	An excellent substrate for Protein Tyrosine Phosphatase 1B (Cat. No. 539735) (k_{cat}/K_m = 2.2 X $10^7 M^{-1}s^{-1}$). Substrate hydrolysis is measured by the increase in tyrosine fluorescence, which can be continuously monitored at 305 nm following excitation at 280 nm. *Purity:≥98% by HPLC.* M.W. 1359.4	1 mg	
Protein Tyrosine Phosphatase Substrate II (TRDIpYETDpYpYRK)	539738	An excellent protein tyrosine phosphatase substrate. The sequence is derived from the insulin receptor β-subunit cytoplasmic domain containing the regulatory autophosphorylation sites Tyr^{1146}, Tyr^{1150}, and Tyr^{1151}. *Purity:≥98% by HPLC.* M.W. 1862.7	500 µg	
Protein Tyrosine Phosphatase Substrate I (ENDpYINASL)	539750	An excellent substrate for the detection and characterization of a wide variety of intracellular and receptor-linked protein tyrosine phosphatases, particularly when limiting amounts of tissue extracts or immunoprecipitates are available. *Purity:≥90% by HPLC.* M.W. 1118.1	500 µg	

Protein Tyrosine Phosphatase Inhibitors

Product	Cat. No.	Comments	Size	Price
bpV(bipy)	203694	A potent protein tyrosine phosphatase (PTP) inhibitor (K_i = 100 nM for insulin receptor dephosphorylation). Also reported to be a potent inhibitor of PTEN (IC_{50} = 18 nM). *Purity: ≥95% by ^{51}V-NMR.* M.W. 380.3	5 mg	
bpV(HOpic)	203701	A potent protein tyrosine phosphatase (PTP) inhibitor. Also reported to potently inhibit PTEN (IC_{50} = 14 nM). *Purity:≥90% by ^{51}V-NMR.* M.W. 419.3	5 mg	
bpV(phen)	203695	A potent protein tyrosine phosphatase (PTP) inhibitor. Exhibits 1000-fold potency over sodium orthovanadate. Also reported to potently inhibit PTEN (IC_{50} = 38 nM). *Purity:≥99% by ^{51}V-NMR.* M.W. 404.3	10 mg	
bpV(pic)	203705	A potent protein tyrosine phosphatase (PTP) inhibitor. Also reported to potently inhibit PTEN (IC_{50} = 31 nM). *Purity:≥95% by ^{51}V-NMR.* M.W. 367.3	5 mg	
Dephostatin	263200	A protein tyrosine phosphatase (PTP) inhibitor (IC_{50} = 7.7 µM). *Purity:≥90% by HPLC.* M.W. 168.2	1 mg	
3,4-Dephostatin, Ethyl-	263203	A more stable ethyl analog of the protein tyrosine phosphatase (PTP) inhibitor 3,4-Dephostatin (Cat. No. 263202). Potently inhibits PTP1B (IC_{50} = 3.18 µM). *Purity:≥90% by HPLC.* M.W. 182.2	1 mg	

Protein Tyrosine Phosphatase-1B

Protein Tyrosine Phosphatase Inhibitors *(continued)*

Product	Cat. No.	Comments	Size	Price
mpV(pic)	475950	A potent PTP inhibitor. More potent for insulin receptor (IR) dephosphorylation than EGFR dephosphorylation. An excellent insulin mimetic. *Purity:≥90% by ^{51}V-NMR.* M.W. 257.1	10 mg	
Phenylarsine Oxide	521000	A cell-permeable protein tyrosine phosphatase inhibitor (IC_{50} = 18 µM). Stimulates 2-deoxyglucose transport in insulin-resistant human skeletal muscle and activates $p56^{lck}$ protein tyrosine kinase. *Purity:≥95% by elemental analysis.* M.W. 168.0	250 mg	
PTP1B Inhibitor	539741	A selective, reversible and non-competitive allosteric inhibitor of PTP1B (IC_{50} = 4 µM and 8 µM for $PTP1B_{403}$ and $PTP1B_{298}$, respectively). *Purity:≥95% by HPLC.* M.W. 741.5	5 mg	
Protein Tyrosine Phosphatase CD45 Inhibitor	540215	A cell-permeable, potent, selective, competitive, and reversible inhibitor of CD45. Has minimal effect on PTPIB (IC_{50} <30 µM using phosphorylated Ick^{505} peptide as a substrate). *Purity:≥97% by HPLC.* M.W. 307.3	1 mg	
Protein Tyrosine Phosphatase Inhibitor I	540200	A potent, cell-permeable, covalent PTP inhibitor. Inhibits SHP-1 (K_i = 43 µM) and PTP-1B (K_i = 42 µM). *Purity:≥95% by HPLC.* M.W. 215.1	10 mg	
Protein Tyrosine Phosphatase Inhibitor II	540205	A potent, cell-permeable, covalent PTP inhibitor. Binds to SHP-1 and inhibits its activity (K_i = 128 nM). *Purity:≥98% by GC.* M.W. 229.1	25 mg	
Protein Tyrosine Phosphatase Inhibitor III	540210	A potent, cell-permeable, covalent PTP inhibitor. Binds to SHP-1 and inhibits its activity (K_i = 193 µM). *Purity:≥90% by HPLC.* M.W. 273.1	10 mg	
Protein Tyrosine Phosphatase Inhibitor IV	540211	A potent, reversible, substrate competitive, active-site-directed inhibitor of protein tyrosine phosphatases (PTP). Reported to inhibit SHP-2 (IC_{50} = 1.8 µM), PTP1B (IC_{50} = 2.5 µM), PTP-ε (IC_{50} = 8.4 µM), PTP-Meg-2 (IC_{50} = 13 µM), PTPσ (IC_{50} = 20 µM), PTP-β (IC_{50} = 6.4 µM), and PTP-µ (IC_{50} = 6.7 µM). *Purity:≥95% by HPLC.* M.W. 608.6	10 mg	
Sodium Orthovanadate	567540	Inhibitor of protein tyrosine phosphatases of general/broad specificity; potent inhibitor of alkaline phosphatase. M.W. 183.9	5 g	
Phosphotyrosine Phosphatase Inhibitor Set (Vanadium)	525325	Contains 5 g of Sodium Orthovanadate (Cat. No. 567540), 10 mg each of bpV(phen) (Cat. No. 203695), and mpV(pic) (Cat. No. 475950).	1 set	
Phosphatase Inhibitor Cocktail Set II	524625	A cocktail of five inhibitors of acid and alkaline phosphatases as well as protein tyrosine phosphatases. Suitable for use with tissue and cell extracts, including extracts containing detergents. Each vial contains 200 mM Imidazole, 100 mM Sodium Fluoride, 11 mM Sodium Molybdate, 100 mM Sodium Orthovanadate, and 400 mM Sodium Tartrate Dihydrate. Dilute 1:100 just prior to use. Note: 1 set = 5 x 1 ml.	1 set	
Phosphatase Inhibitor Cocktail Set III	524627	A cocktail of four phosphatase inhibitors for broad-spectrum inhibition of both serine/threonine and protein tyrosine phosphatases. Each vial contains 1 ml of aqueous solution with the following components: 50 mM Sodium Fluoride, 10 mM β-Glycerophosphate (Cat. No. 356756), 10 mM Sodium Pyrophosphate Decahydrate, 1 mM Sodium Orthovanadate. Note: 1 set = 5 x 1 ml.	1 ml 1 set	

Glycogen Synthase Kinase-3

Glycogen synthase kinase-3 (GSK-3), a multifunctional serine/threonine kinase, is a key regulator of numerous signaling pathways. Two isoforms of GSK-3 are reported in mammals: a 51 kDa GSK-3α and a 47 kDa GSK-3β that exhibit about 98% homology in their kinase domains. Several known GSK-3 substrates participate in a wide spectrum of cellular processes, including glycogen metabolism, transcription, translation, cytoskeletal regulation, intracellular vesicular transport, cell cycle progression, stem cell renewal, and apoptosis.

GSK-3 is normally active in cells and is regulated through inhibition of its activity. For example, insulin treatment causes its inactivation through a PI 3-kinase (PI 3-K)-dependent mechanism. PI 3-K-induced activation of PKB/Akt results in phosphorylation of Ser^{21} on GSK-3α and Ser^{9} on GSK-3β, which inhibit GSK-3 activity. This prevents phosphorylation of substrates, such as glycogen synthase, and allows them to be activated. GSK-3 also plays a key inhibitory role in the Wnt signaling pathway. β-catenin is shown to be a primed substrate for GSK-3, with casein kinase I (CKI) acting as the priming kinase. In unstimulated cells, CKI phosphorylates β-catenin on Ser^{45}, priming it for further phosphorylation on $Ser^{33, 37, and 41}$ by GSK-3, thereby allowing β-catenin to be ubiquitinated for proteasomal degradation. However, unphosphorylated β-catenin translocates to the nucleus where it transactivates genes regulated by TCF/LEF transcription factors.

GSK-3 shows a preference for target proteins that are pre-phosphorylated at a `priming' residue located C-terminal to the site of GSK-3 phosphorylation. Priming phosphorylation, although not absolutely required, enhances the efficiency of phosphorylation of most GSK-3 substrates by about 100-fold. Although phosphorylation of a Thr residue in the activation loop (T-loop) is shown to be essential for several closely related protein kinases, such as Cdk2, p38γ, and ERK2, the T-loop of GSK-3 does not undergo any Thr phosphorylation. The function of missing pThr in the T-loop of GSK-3 is carried out by the phosphorylated residue of a primed substrate that binds to a positively charged pocket consisting of Arg^{96}, Arg^{180}, and Lys^{205} (for GSK-3β). Arg^{96} is shown to be a crucial component of the positive pocket that binds primed substrates. Arg^{96} to Ala^{96} mutation disrupts the pocket in a way that primed substrates can no longer bind and, hence, the enzyme remains active. Also, Ser^{9}-phosphorylated pseudosubstrate is no longer capable of inactivating the enzyme. Small molecule inhibitors that fit in the positively charged pocket of the kinase domain of GSK-3 are useful for selectively inhibiting primed substrates.

GSK-3 can be considered as a target for both metabolic and neurological disorders. Abnormalities in pathways that use GSK-3 as a regulator have been linked to several disease conditions. Hence, GSK-3 has emerged as a potential therapeutic target, particularly in non-insulin-dependent diabetes mellitus, Alzheimer's disease, developmental disorders, and cancer. Despite their chemical diversity, most inhibitors of GSK-3 act by competing with ATP for the ATP-binding site. Since ATP-binding pockets of GSK-3α and GSK-3β are identical, it has been a real challenge to develop isozyme specific inhibitors. Inhibitors belonging to aloisines, the paullones, and the maleimide families, have shown promise as therapeutic agents. Due to its involvement in multiple pathways, selectivity of GSK-3 inhibition is an important factor in the development of inhibitors for therapeutic applications.

Glycogen Synthase Kinase-3

Antibodies

PhosphoDetect™ Anti-Glycogen Synthase (pSer$^{645/649/653/657}$) Rabbit pAb

Polyclonal IgG, undiluted serum. Immunogen: a synthetic peptide corresponding to amino acids 642-661 of human glycogen synthase. Reacts with human. **IB, PS**

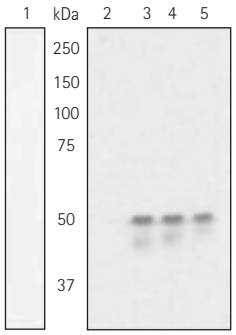
Cat. No. PC746 5 µl
25 µl

Detection of human glycogen synthase, phosphorylated on Ser645/649/653/657, by staining paraffin sections. Sample: Prostate tissue. Primary antibody: PhosphoDetect™ Anti-Glycogen Synthase (pSer) Rabbit pAb (Cat. No. PC746) (1:2000). Detection: DAB with methyl green counterstain.

PhosphoDetect™ Anti-Glycogen Synthase Kinase-3β, (pSer^{9}) Rabbit pAb

Polyclonal IgG, immunoaffinity, purified. Immunogen: a synthetic phosphopeptide corresponding to amino acids surrounding Ser^{9} in human GSK-3β. Recognizes the ~47 kDa GSK-3β protein phosphorylated on Ser^{9} in insulin or IGF-1 treated, serum-starved 3T3-L1 cells. Reacts with human, rat. **IB**

Cat. No. PS1018 10 T

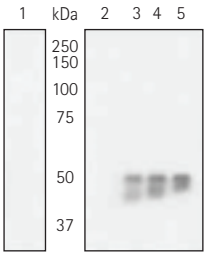


Detection of human GSK-3β, phosphorylated on Ser^{9}, by immunoblotting. Samples: Control lysate (lane 1) or control lysated spiked with recombinant GSK-3β (lanes 2-5). Primary antibody: PhosphoDetect™ Anti-Glycogen Synthase Kinase-3b (pSer^{9}) Rabbit pAb (Cat. No. PS1018) (1:1000) preincubated without peptide (lanes 1,5) or with phosphopeptide immunogen (lane 2), non-phosphopeptide corresponding to the immunogen (lane 3), or a generic phosphoserine-containing peptide (lane 4). Detection: chemiluminescence.

PhosphoDetect™ Anti-Glycogen Synthase Kinase-3α/β (pTyr$^{279/216}$) Rabbit pAb

Polyclonal, IgG, purified. Immunogen: A synthetic peptide surrounding Tyr$^{279/216}$ phosphorylation sites of human GSK3α/β. Recognizes the ~51 kDa GSK-3α protein phosphorylated at Tyr^{279} and the ~47 kDa protein GSK-3β phosphorylated at Tyr^{216}. Reacts with human, mouse, rat. **DB, ELISA, IB, IC**

Cat. No. ST1013 10 T



Detection of human GSK-3β phosphorylated on Tyr^{216} by immunoblotting. Samples: Cell lysates from control cells (lane 1) or control lysates containing human recombinant GSK-3β (lanes 2-5). Primary antibody: PhosphoDetect™ Anti-Glycogen Synthase Kinase-3α/β (pTyr$^{279/216}$) Rabbit pAb (Cat. No. ST1013) (1:1000) pre-incubated without peptide (lanes 1, 5), with phosphopeptide immunogen (lane 2), a generic phosphoserine-containing peptide (lane 3), and non-phosphopeptide corresponding to the immunogen (lane 4). Detection: chemiluminescence.

Anti-Glycogen Synthase Kinase 3β, C-Terminal (334-348) Rabbit pAb

Polyclonal IgG, purified. Immunogen: a synthetic peptide corresponding to amino acids 334-348 of rat GSK-3β kinase subdomain XI, conjugated to KLH. Recognizes the ~47 kDa GSK-3β in a variety of rat and mouse tissues as well as in human thymus and HeLa cells. Reacts with human, mouse, and rat. **ELISA, IB, IP**

Cat. No. 361528 100 µg

PhosphoDetect™ Anti-Glycogen Synthase Kinase 3β (pSer^{9}) Mouse mAb (2D3)

Monoclonal IgG$_1$, purified. Immunogen: a synthetic phosphopeptide surrounding the Ser^{9} phosphorylation site of human GSK-3β. Recognizes the ~47 kDa GSK-3β phosphorylated at Ser^{9}. Supplied with a control lysate derived from 2 x 10^{6} EGF-treated HepG2 cells. Reacts with human, and mouse. **ELISA, IB**

Cat. No. 361527 1 set

DB: dot blot; **ELISA**: enzyme-linked immunosorbent assay; **IB**: immunoblotting; **IC**: immunocytochemistry; **IP**: immunoprecipitation; **mAb**: monoclonal; **pAb**: polyclonal; **PS**: paraffin sections

Antibodies *(continued)*

Anti-Glycogen Synthase Kinase-3α/β Mouse mAb (1H8)

Monoclonal IgG_{2a}, purified. Immunogen: recombinant *Xenopus laevis* GSK3β. Recognizes the ~51 kDa GSK3α and ~47 kDa GSK3β proteins. Reacts with bovine, canine, hamster, human, mouse, ovine, porcine, rabbit, and rat. **ELISA, IB**

Cat. No. 368662 100 µg

PhosphoDetect™ Anti-Glycogen Synthase Kinase-3β (pSer^9) (Ab-1) Rabbit pAb

Polyclonal IgG, purified. Immunogen: a synthetic phosphopeptide surrounding the Ser^9 phosphorylation site of human GSK-3β protein. Recognizes the ~47 kDa GSK-3β protein phosphorylated at Ser^9. Reacts with human, rat, and *Xenopus*. **DB, ELISA, IB**

Cat. No. PC242 50 µg

DB: dot blot; **ELISA**: enzyme-linked immunosorbent assay; **IB**: immunoblotting; **mAb**: monoclonal; **pAb**: polyclonal

Enzymes

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

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

Cat. No. 361526 5 KU

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

A dual specificity kinase that plays important roles in insulin-and Wnt signaling. Its known substrates include glycogen synthase, p90^{rsk}, Tau, c-Jun, and CREB. This recombinant kinase contains both an N- and a C-terminal His•Tag® sequence. *Biological activity: 1 µg GSK-3β phosphorylates 100 ng Tau protein in 30 min at 30˚C, pH 7.5. Purity: ≥90% by SDS-PAGE.* M.W. 46,000

Cat. No. 361524 100 µg

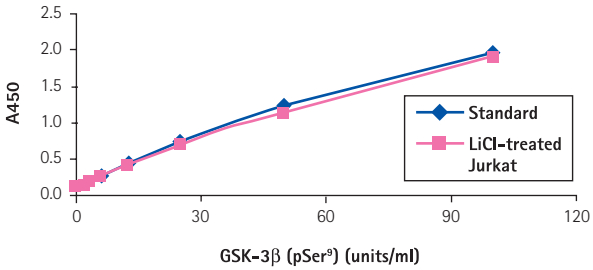
GSK-3 Assay Kits

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

Format: 96-well plate
Sensitivity: < 0.4 U/ml
Assay time: 4 h

Detects and quantifies the level of GSK-3β (glycogen synthase kinase-3beta) phosphorylated at Ser^9 in human, mouse, and rat cells. GSK-3 plays an important role in diabetes, stroke, and Alzheimer's disease.

Cat. No. CBA069 1 kit



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

GSK-3β ELISA Kit

Format: 96-well plate
Sensitivity: < 0.26 ng/ml
Assay time: 4 h

Detects and quantifies the level of GSK-3β protein independent of its phosphorylation state in human, mouse and rat cells.

Cat. No. CBA068 1 kit

Glycogen Synthase Kinase-3

GSK-3 Substrate

GSK-3β Substrate (GPHRSTPESRAAV)

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, or Casein Kinase II. Undergoes phosphorylation at the Ser^{353} and Ser^{357} sites. *Purity:* ≥ *95% by HPLC.* M.W. 1364.5

Cat. No. 361530 1 mg

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

GSK-3 Inhibitors

Product	Cat. No.	Comments	Size	Price
Aloisine A	128125	A potent, cell permeable, selective, reversible, and ATP-competitive inhibitor of GSK-3 (IC_{50} = 500 nM for GSK-3α and 1.5 µM for GSK-3β). Also inhibits Cdks (IC_{50} = 150 nM for Cdk1/cyclin B, 120 nM for Cdk2/cyclin A, 400 nM for Cdk2/cyclin E, and 160 nM for Cdk5/p35, JNK (IC_{50} ~3–10 µM), ERKs (IC_{50} = 18 µM for ERK1 and 22 µM for ERK2), PIM1 (IC_{50} >10 µM), and insulin receptor tyrosine kinase (IC_{50} = 60 µM). *Purity:*≥*95% by HPLC.* M.W. 267.3	5 mg	
1-Azakenpaullone	191500	A Kenpaullone (Cat. No. 422000) analog. A potent, ATP-competitive inhibitor of GSK-3β (IC_{50} = 18 nM). *Purity:*≥*95% by HPLC.* M.W. 328.2	1 mg	
Aloisine, RP106	128135	A cell-permeable, pyrrolo-pyrazine compound that acts as a potent, selective ATP-competitive inhibitor of GSK-3 (IC_{50} = 920 nM) and Cdk1/cyclin B (IC_{50} = 700 nM), Cdk5/p25 (IC_{50} = 1.5 µM) . *Purity:*≥*95% by HPLC.* M.W. 281.4	5 mg	
Alsterpaullone	126870	Acts as a potent inhibitor of Cdk1/cyclin B (IC_{50} = 35 nM). Also inhibits the activity of Cdk5/p25-dependent phosphorylation of DARPP-32. One of the most active paullones that acts by competing with ATP for binding to GSK-3β and inhibits the phosphorylation of tau. *Purity:*≥*95% by HPLC.* M.W. 293.3	1 mg	
FRATtide	344265	An inhibitor of GSK-3 (IC_{50} = 500 nM for GSK-3α and 1.5 µM for GSK-3β). Also acts as a potent, selective, reversible, and ATP-competitive inhibitor of Cdks (IC_{50} = 150 nM for Cdk1/cyclin B, 120 nM for Cdk2/cyclin A, 400 nM for Cdk2/cyclin E, and 160 nM for Cdk5/p35). Purity: ≥95% by HPLC. M.W. 4534.1	500 µg	
GSK-3β Inhibitor I	361540	A thiadiazolidinone analog that acts as a highly selective, non-ATP competitive inhibitor of GSK-3β (IC_{50} = 2 µM). Proposed to bind to the active site of GSK-3β. Does not affect the activity of Cdk1/cyclin B. *Purity:*≥ *95% by HPLC.* M.W. 222.3	5 mg	
GSK-3β Inhibitor II	361541	A 2-thio-[1,3,4]-oxadiazole-pyridyl derivative that acts as a potent inhibitor of GSK-3β (IC_{50} = 390 nM). *Purity:*≥*95% by HPLC.* M.W. 395.2	5 mg	
GSK-3β Inhibitor III	361542	An oxothiadiazolidine-3-thione analog that acts as a non-ATP competitive inhibitor of GSK-3β (IC_{50} = 10 µM). *Purity:*≥*95% by HPLC.* M.W. 314.4	1 mg	
GSK-3β Inhibitor VI	361547	A cell-permeable, irreversible, non-ATP competitive inhibitor of GSK-3β (IC_{50} = 1 µM). *Purity:*≥*95% by HPLC.* M.W. 318.4	5 mg	
GSK-3β Inhibitor VII	361548	A cell-permeable, selective, irreversible, and non-ATP competitive inhibitor of GSK-3β (IC_{50} = 500 nM). *Purity:*≥*95% by HPLC.* M.W. 277.9	5 mg	
GSK-3β Inhibitor VIII	361549	A cell-permeable, potent, and highly specific inhibitor of glycogen synthase kinase-3β (GSK-3β) (IC_{50} = 104 nM). Inhibition is competitive with respect to ATP (K_i = 38 nM). *Purity:*≥*95% by HPLC.* M.W. 308.3	5 mg	
GSK-3 Inhibitor IX, Bio	361550	A cell-permeable, highly potent, selective, reversible, and ATP-competitive inhibitor of GSK-3α/β (IC_{50} = 5 nM). At higher concentrations, inhibits Cdk2/cyclin A (IC_{50} = 300 nM) and Cdk5/p25 (IC_{50} = 83 nM). *Purity:*≥*97% by HPLC.* M.W. 356.2	1 mg	
InSolution™ GSK-3 Inhibitor IX	361552	A 10 µM (500 µg / 140 µL) solution of GSK-3 Inhibitor IX (Cat. No. 361550) in DMSO. *Purity:*≥*97% by HPLC.* M.W. 356.2	500 µg	
GSK-3 Inhibitor IX, Control, MeBIO	361556	A cell-permeable N-methylated analog of GSK-3 Inhibitor IX, BIO (Cat. No. 361550) that serves as a relevant kinase inactive control (IC_{50} > 92 µM for Cdk1/B, and > 100 µM for Cdk5/p25 and GSK-3α/β). *Purity:*≥*97% by HPLC.* M.W. 370.2	1 mg	
GSK-3 Inhibitor X	361551	Exhibits greater selectivity for GSK-3α/β (IC_{50} = 10 nm) over Cdk5/p25, Cdk2/A and Cdk1/B (IC_{50} = 2.4 µM, 4.3 µM and 63 µM, respectively). *Purity:*≥*95% by HPLC.* M.W. 398.2	1 mg	

GSK-3 Inhibitors *(continued)*

Product	Cat. No.	Comments	Size	Price
GSK-3β Inhibitor XI	361553	A cell-permeable, potent, specific, ATP-competitive inhibitor of GSK-3β (K_i = 25 nM). *Purity:≥95% by HPLC.* M.W. 349.3	1 mg	
GSK-3β Inhibitor XII, TWS119	361554	A cell-permeable pyrrolopyrimidine compound that acts as a potent and selective inhibitor of GSK-3β (IC_{50} = 30 nM). Binds to GSK-3β with high-affinity (K_d = 126 nM). *Purity:≥95% by HPLC.* M.W. 318.3	1 mg 5mg	
GSK-3 Inhibitor XIII	361555	An aminopyrazole compound that acts as a potent and ATP-binding site inhibitor of GSK-3 (K_i = 24 nM). *Purity:≥95% by HPLC.* M.W. 301.4	1 mg 5mg	
GSK-3β Peptide Inhibitor	361545	A phosphorylated peptide that acts as a substrate-specific, competitive inhibitor of GSK-3β (IC_{50} = 150 µM). Inhibits Cdc2, CK II, MAPK, PKA, PKB, and PKCδ at higher concentrations (200 µM results in 85–100% inhibition). *Purity:≥95% by HPLC.* M.W. 1197.3	1 mg	
GSK-3β Peptide Inhibitor, Cell-permeable	361546	A cell-permeable, myristoylated form of GSK-3β Peptide Inhibitor (Cat. No. 361545) with a glycine spacer. Acts as a selective, substrate-specific, competitive inhibitor of GSK-3β (IC_{50} = 40 µM). Does not affect the activities of Cdc2, PKB, or PKC. *Purity:≥98% by HPLC.* M.W. 1464.7	1 mg	
Indirubin-3′-monoxime	402085	A potent cell-permeable inhibitor of GSK-3β (IC_{50} = 22 nM) and Cdks (IC_{50} = 180 nM for Cdk1 and 100 nM for Cdk5). *Purity:≥ 98% by HPLC.* M.W. 277.3	1 mg	
Indirubin-3′-monoxime, 5-Iodo-	402086	A highly potent, cell-permeable inhibitor of GSK-3β (IC_{50} = 9 nM) and Cdk1 (IC_{50} = 25 nM) and Cdk5 (IC_{50} = 20 nM). Inhibition is competitive with respect to ATP. *Purity:≥97% by HPLC.* M.W. 403.2	1 mg	
Indirubin-3′-monoxime-5-sulphonic Acid	402088	A potent and selective inhibitor of GSK-3β (IC_{50} = 80 nM). Also inhibits Cdk1 and Cdk5 (IC_{50} = 5 nM for Cdk1; IC_{50} = 7 nM for Cdk5). Inhibition is competitive with respect to ATP. *Purity:≥97% by HPLC.* M.W. 357.3	1 mg	
Kenpaullone	422000	A potent, cell-permeable, ATP competitive inhibitor of GSK-3β (IC_{50} = 230 nM), Lck (IC_{50} = 470 nM) and Cdks. Inhibits Cdk1/cyclin B (IC_{50} = 400 nM), CdK2/cyclin A (IC_{50} = 680 nM), Cdk2/cyclin E (IC_{50} = 7.5 µM), and Cdk5/p25 (IC_{50} = 850 nM). Also inhibits c-Src (IC_{50} - 15 µM), casein kinase II (IC_{50} = 20 µM), ERK1 (IC_{50} = 20 µM), and ERK2 (IC_{50} = 9 µM) at higher concentrations. *Purity:≥95% by HPLC.* M.W. 327.2	1 mg	
Ro-31-8220	557520	A cell-permeable, competitive, inhibitor of GSK-3 in primary adipocytes (IC_{50} = 6.8 nM) and in GSK-3β immunoprecipitates (IC_{50} 2.8 nM). Also inhibits protein kinase C (PKC; IC_{50} = 10 nM) over CaM kinase II (IC_{50} = 17 µM) and protein kinase A (IC_{50} = 900 nM). *Purity:≥95% by HPLC.* M.W. 553.7	500 µg	

Lipids in Diabetes and Obesity

Antibodies to Apolipoproteins and Lipoproteins

Product	Cat. No.	Comments	Size	Price
Anti-Apolipoprotein A-I Goat pAb	178463	Immunogen: purified human apolipoprotein A-I. Recognizes human apolipoprotein A-I. **IB, IEP, IP, PS**	1 ml	
Anti-Apolipoprotein A-I Mouse mAb (412)	178474	Monoclonal IgG_1. Immunogen: full length human apolipoprotein A-I. Recognizes human apolipoprotein A-I. **EIA, ELISA, RIA**	1 mg	
Anti-Apolipoprotein A-I Mouse	178472	Monoclonal IgG_1, purified. Immunogen: full length human apoliprotein A-I. Recognizes human apolipoprotein A-I. **EIA, ELISA, RIA**	1 mg	
Anti-Apolipoprotein B Mouse mAb	178444	Monoclonal IgG_1, purified. Immunogen: purified LDL from human serum. Recognizes human apolipoprotein B. **EIA, ELISA, RIA**	1 mg	
Anti-Apolipoprotein A-I Mouse mAb (6001)	178470	Monoclonal, IgG_{2a}, purified. Immunogen: full length human apolipoprotein A-I. Recognizes human apolipoprotein A-I. **EIA, ELISA, RIA**	1 mg	
Anti-Apolipoprotein A-I Rabbit pAb	178422	Polyclonal IgG, purified. Immunogen: full length human apolipoprotein A-I. Recognizes human apolipoprotein A-I. **ELISA, IB**	1 ml	
Anti-Apolipoprotein B Goat pAb	178467	Polyclonal IgG, diluted serum. Immunogen: purified human apolipoprotein B. Recognizes human apolipoprotein B. **IEP, IP**	1 ml	
Anti-Apolipoprotein B Mouse mAb (F_2C_9)	178446	Monoclonal IgG_1 purified. Immunogen: purified LDL from human serum. Recognizes human apolipoprotein B. **EIA, ELISA, RI**A	1 mg	
Anti-Apolipoprotein C-II Rabbit pAb	178428	Polyclonal IgG, purified. Immunogen: human apolipoprotein C-II. Recognizes human apolipoprotein C-II. **ELISA, IB**	1 ml	
Anti-Apolipoprotein E Goat pAb	178479	Polyclonal IgG, serum. Immunogen: purified recombinant human apolipoprotein E. Recognizes human apolipoprotein E. **ELISA, IB, IP**	500 µl	
Anti-Apolipoprotein E Mouse mAb (E6D7)	NE1004	Monoclonal IgG_1. Immunogen: a synthetic peptide corresponding to amino acids surrounding the polymorphic amino acid position 158 of ApoE. Recognizes the ~35 kDa E2, E3, and E4 isoforms of apolipoprotein E in human serum and brain. **ELISA, FS, IB, IP, PS**	100 µl	
Anti-Cu^{2+}-Oxidized Low Density Lipoprotein Rabbit pAb	428033	Polyclonal IgG, undiluted serum. Immunogen: fully Cu^{2+}-oxidized human low density lipoprotein. Recognizes both fully oxidized modifications of LDL and minimally oxidized LDL, but the reaction to native LDL is weak. Reacts with a wide range of species. **ELISA, IH**	100 µl	
Anti-HOCl-Oxidized Low Density Lipoprotein Rabbit pAb	428035	Polyclonal IgG, undiluted serum. Immunogen: a human hypochlorite-modified low-density lipoprotein. Recognizes HOCl-LDL. Weakly cross-reacts with HNE-LDL. Reacts with a wide range of species. **ELISA, FS, PS**	100 µl	

EIA: enzyme immunoassay; **ELISA**: enzyme-linked immunosorbent assay; **FS**: frozen sections; **IB**: immunoblotting; **IEP**: immunoelectrophoresis; **IH**: immunohistochemistry; **IP**: immunoprecipitation; **mAb**: monoclonal; **pAb**: polyclonal; **PS**: paraffin sections; **RIA**: radioimmunoassay

Apolipoproteins and Lipoproteins

Product	Cat. No.	Comments	Size	Price
Apolipoprotein A-I, Human Plasma, High-Density Lipoprotein	178452	Functions as a cofactor for lecithin-cholesterol acyltransferase (LCAT). Plays an important role in HDL metabolism. *Purity:≥95% by SDS-PAGE.* M.W. 28,000	500 µg	
Apolipoprotein A-II, Human Plasma, High-Density Lipoprotein	178455	Shown to bind to phospholipids during lipoprotein metabolism. Displaces lecithin-cholesterol acyltransferase bound to lipoprotein. Influences HDL functional states and contributes to arteriosclerosis. *Purity:≥95% by SDS-PAGE.* M.W. 17,380	500 µg	
Apolipoprotein B, Human Plasma, Low-Density Lipoprotein	178456	Produced by the liver, and is a dominant protein constituent of LDL that is also present in VLDL. Ligand for LDL receptor, directing clearance of LDL from plasma to the liver. Functions as a cofactor in enzymatic reactions. Mean serum concentration: 950 µg/ml. Higher levels are reported in familial hyperlipidemia, obesity, and diabetes. *Purity:≥95% by SDS-PAGE.* M.W. 550,000	500 µg	
Apolipoprotein C-I, Human Plasma, Very Low-Density Lipoprotein	178459	A major component of VLDL that partially activates lecithin-cholesterol acyltransferase activity and inhibits lipoprotein lipase activity. *Purity:≥95% by SDS-PAGE.* M.W. 6613	100 µg	
Apolipoprotein C-II, Human Plasma, Very Low-Density Lipoprotein	178462	Found primarily in VLDL and chylomicrons. Functions as a cofactor for lipoprotein lipase. Elevated serum levels of Apo C-II are common in type I, III, IV, and V hyperlipoproteinemia. Low serum concentrations of Apo C-II are indicative of nephrotic syndrome (Tangier's Disease). *Purity:≥95% by SDS-PAGE.* M.W. 8800	50 µg	
Apolipoprotein C-III, Human Plasma, Very Low-Density Lipoprotein	178461	Major protein of VLDL and chylomicrons. Involved in the uptake of triglycerides by cells. May inhibit the activation of lipoprotein lipase by Apo C-II. Present in normal plasma at 80-150 µg/ml. *Purity:≥95% by SDS-PAGE.* M.W. 8750	100 µg	
Apolipoprotein E, Human Plasma, Very Low-Density Lipoprotein	178468	A component of VLDL and a subclass of HDL. Serves as a ligand for LDL receptors, where it participates in the transport and redistribution of cholesterol and other lipids. Also functions in immunoregulation, cell growth, and differentiation. Present in normal plasma at concentrations of 50 µg/ml. Purity: ≥95% by SDS-PAGE. M.W. 34,200	50 µg	

Apolipoproteins and Lipoproteins *(continued)*

Product	Cat. No.	Comments	Size	Price
Apolipoprotein E, Isoform E2, Human, Recombinant, Insect Cells	178480	Isoform bearing cysteine at amino acids 112 and 158. Binds to β-amyloid protein but not to the LDL receptor. Does not compete with human low density lipoprotein for binding to the human Apo B/E (LDL) receptor. Produced by expression in a baculovirus-based insect cell system. *Purity:≥95% by SDS-PAGE.* M.W. 34,000	50 µg	
Apolipoprotein E, Isoform E3, Human, Recombinant, Insect Cells	178475	Isoform bearing cysteine at amino acid 112 and arginine at amino acid 158. Most common form of apolipoprotein E. Binds to β-amyloid protein and to the LDL receptor. Produced by expression in a baculovirus-based insect cell system. *Purity:≥95% by SDS-PAGE.* M.W. 36,150	50 µg	
Apolipoprotein E, Isoform E4, Human, Recombinant, Insect Cells	178476	Isoform bearing arginine at amino acid residues 112 and 158. Binds to the LDL receptor, and binds to β-amyloid protein with higher affinity than Apo E2 and E3. Significantly higher levels of E4 are reported in patients with Alzheimer's Disease and atherosclerosis. Promotes early appearance of β-amyloid and neurofibrillary tangles in the elderly. Produced by expression in a baculovirus-based insect cell system. *Purity:≥95% by SDS-PAGE.* M.W. 34,000	50 µg	
Lipoproteins, High Density, Human Plasma	437641	Cholesterol-carrier lipoprotein that acts as scavenger of tissue cholesterol. Important in cholesterol efflux from tissues. Involved in return of cholesterol from the periphery to the liver for removal as bile acids. *Composition: 50% lipid, 50% protein. Purity:≥95% of total lipoprotein content by electrophoresis.*	10 mg	
Lipoproteins, Low Density, Human Plasma	437644	Cholesterol-carrier lipoprotein responsible for delivery of lipids (cholesterol) from liver to tissues. *Composition: 78 - 81% lipid; 19 - 22% protein. Purity:≥95% of total lipoprotein content by electrophoresis*	10 mg	
Lipoproteins, Very Low Density, Human Plasma	437647	VLDL transports liver-synthesized triglycerides and cholesterol. May counteract the inhibitory effect of glucocorticoids on arachidonic acid release and prostaglandin I_2 formation in vascular smooth muscle cells. *Composition: 88-95% lipid; 5-12% protein. Purity:≥95% of total lipoprotein content by electrophoresis.*	5 mg	

PHM-L LIPOSORB™ Absorbent

Designed to selectively remove lipoproteins from plasma or serum by batch procedure or column chromatography; antibody content and coagulation factors remain intact. Is directly applicable with no further additions, affording improved serum or plasma stability. Has very low solubility in most solvents and has excellent chemical stability in acids and bases. PHM-L LIPOSORB™ Absorbent is resistant to enzymatic degradation and to activation of coagulation factors. Is heat stable and can be sterilized by autoclaving (120˚C) without altering its binding capacity. Has high capacity with no volume limitation and is simple to use without expensive apparatus. Offers significant technical advantages over phenylagarose. One gram of absorbent is sufficient to remove lipids from 25 ml of serum or ascites.

Cat. No. 524371 1 g
10 g

Kits

Cholesterol/Cholesteryl Ester Quantitation Kit

Format: 96-well plate
Assay range: 0.02-10 µg/well
Sample type: Cells, tissues, serum

A sensitive colorimetric or fluorometric assay for the quantitative measurement of cholesterol, cholesteryl ester, or both by spectrophotometry ($A_{570\ nm}$) or fluorometry at Ex/Em =535/587 nm. The fluorometric assay can detect 0.02-1 µg/well and is 4-10 fold more sensitive than the colorimetric assay. Suitable for up to 100 tests.

Cat. No. 428901 1 kit

LCAT Activity Assay Kit, Fluorometric

Format: 100 Tests
Assay time: 4.5-8.5 h
Sample type: Plasma

Useful for the quantitative assay of lecithin:cholesterol acyltransferase activity (LCAT) in human plasma. LCAT mediates the formation of cholesteryl esters in human plasma by transferring an acyl chain from the sn-2 position of phosphatidylcholine to cholesterol. Suitable for up to 100 tests.

Cat. No. 428900 1 kit

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Lipids in Diabetes and Obesity

Fatty Acids

Product	Cat. No.	Comments	Size	Price
Arachidonic Acid	181198	Precursor for prostaglandins, prostacyclin, and thromboxane. Binds to G-protein α-subunits in a covalent, post-translational manner. Inhibits Ras-GAP. *Purity:≥99% by TLC and GC.* M.W. 304.5	100 mg 1 g	
Arachidonic Acid, Porcine Liver, Sodium Salt	181205	Precursor for prostaglandins, prostacyclin, and thromboxane. Binds to G-protein α–subunits in a covalent, post-translational manner. Inhibits Ras-GAP. Note: 1 set = 10 x 10 mg. *Purity:≥99% by TLC and GC.* M.W. 326.5	1 set 100 mg	
Linoleic Acid	436305	An essential polyunsaturated ω-3 fatty acid. *Purity:≥97% by GC.* M.W. 280.5	5 g	
Oleic Acid	4954	An essential monounsaturated 18-carbon fatty acid. *Purity:≥99% by GC.* M.W. 282.5	1 g	
Palmitic Acid	506345	A 16-carbon saturated fatty acid. *Purity:≥99% by GC.* M.W. 256.5	25 g 100 g	
Stearic Acid	569398	An 18-carbon saturated fatty acid. *Purity:≥99% by GC.* M.W. 284.5	25 g 100 g	

Sphingolipids

Product	Cat. No.	Comments	Size	Price
Lactosyl Ceramide, Bovine	427572	A neutral glycosphingolipid (GSL) that is the common precursor of the ganglio-, globo-, globoiso-, lacto-, neolacto-, and muco-series of GSL. Promotes a time- and concentration-dependent proliferation of aortic smooth muscle cells via specific activation of p44 MAP kinase. Also stimulates Ras-GTP loading, MEK and Raf kinases, p44 MAP kinase, and c-*fos* expression in human aortic smooth muscle cells. *Purity:≥98% by TLC.* M.W. 960.4	1 mg	
Lactosyl Ceramide, Porcine	219485	A neutral glycosphingolipid reported to activate p44 MAP kinase in aortic smooth muscle cells. Activates NADPH oxidase thereby producing superoxide. *Purity:≥98% by TLC.* M.W. 890.	1 mg	
D-*erythro*-MAPP	454863	A synthetic analog of ceramide. Shown to selectively inhibit alkaline ceramidase both *in vitro* and in intact HL-60 cells (IC_{50} = 1-5 µM for alkaline ceramidase versus IC_{50} > 500 µM for acid ceramidase). This inhibition results in over 3-fold increase in endogenous ceramide in treated cells due to lack of breakdown of ceramide to sphingosine. *Purity:≥98% by NMR.* M.W. 361.6	1 mg	
Sphingomyelin, Bovine Spinal Cord	567706	Contains primarily nervonic and stearic acids. Precursor to ceramide second messengers via the action of sphingomyelinase. *Purity:≥98% by TLC.* M.W. 731.1	100 mg	
D-*erythro*-Sphingosine, Dihydro-	300230	Biosynthetic precursor of sphingosine. Inhibits PKC in Chinese hamster ovary cells (IC_{50} = 2.9 µM). *Purity:≥98% by TLC.* M.W. 301.5	10 mg	
D-*erythro*-Sphingosine, N-Acetyl-	110145	Biologically active, cell-permeable, non-physiological ceramide analog. Inhibits cell growth and induces apoptosis in HL-60 cells. Induces intranucleosomal DNA fragmentation. An activator of heterotrimeric protein phosphatase 2A (PP2A). Stimulates a cytosolic serine/threonine protein phosphatase in T9 cells at concentrations as low as 100 nM. Activates stress activated protein kinase (SAPK) in HL-60 human promyelocytic cells. *Purity:≥98% by TLC.* M.W. 341.5	5 mg	
D-*erythro*-Sphingosine, Dihydro-, N-Acetyl-	219537	May be used as a negative control in studies of C_2 ceramide. Its initial uptake appears to be slower than that of active C_2 ceramide. *Purity: single spot by TLC; 70% erythro, 30% threo.* M.W.299.5	5 mg	
D-*erythro*-Sphingosine, Free Base, Bovine Brain	567725	A potent and selective inhibitor of PKC (PKC; IC_{50} = 2.8 µM) and insulin receptor tyrosine kinase. PKC inhibition is competitive with respect to diacylglycerol, phorbol dibutyrate, and Ca^{2+}. *Purity: single spot by TLC; 70% erythro, 30% threo.* M.W. 299.5	10 mg	
D-*erythro*-Sphingosine, Free Base, High Purity	567726	A highly purified preparation of Cat. No. 567725 containing >99% of the erythro isomer. A potent and selective inhibitor of PKC (IC_{50} = 2.8 µM) and insulin receptor tyrosine kinase. PKC inhibition is competitive with respect to diacylglycerol, phorbol dibutyrate, and Ca^{2+}. *Purity:≥98% by TLC.* M.W. 299.5	10 mg	
D-*erythro*-Sphingosine, N,N-Dimethyl-	310500	A PKC inhibitor (IC_{50} = 12 µM) that also enhances src kinase activity. *Purity:≥98% by TLC.* M.W.327.6	5 mg	

Sphingolipids *(continued)*

Product	Cat. No.	Comments	Size	Price
D-*erythro*-Sphingosine, N-Hexanoyl-	376650	Biologically active, cell-permeable, non-physiological ceramide analog. Induces a dramatic arrest in the G_0/G_1 phase of the cell cycle. Activates MAP kinase. Activates protein phosphatase 2A (PP2A) at 10 nM. Inhibits diacylglycerol accumulation and phospholipase D (PLD) activation in fibroblasts. Induces apoptosis in MOLT-4 leukemia cells. *Purity:≥98% by TLC.* M.W. 397.6	5 mg	
D-*erythro*-Sphingosine, N-Octanoyl-	219540	A short chain cell-permeable analog of endogenous ceramide. Shown to induce apoptosis in a variety of cell lines and to activate MAP kinase in HL-60 cells. *Purity:≥98% by TLC.* M.W.425.7	5 mg	
D-*erythro*-Sphingosine, N-Palmitoyl-	506420	Higher levels of C_{16} ceramide are reported in apoptotic cells. Plays a role in the effector (mitochondrial) phase of apoptosis. *Purity:≥98% by TLC.* M.W. 537.9	5 mg	
D-*erythro*-Sphingosine-1-phosphate	567727	A putative second messenger that mobilizes calcium from intracellular stores via an IP_3-independent pathway. Also stimulates growth of quiescent Swiss/3T3 fibroblasts. Inhibits activation of caspases that cleave PARP and lamins during Fas- and ceramide-mediated apoptosis. *Purity:≥95% by TLC.* M.W. 379.5	1 mg	
Sphingosylphosphorylcholine	567735	The deacylated derivative of sphingomyelin known to accumulate in neuropathic Niemann-Pick disease type A. A potent mitogen that increases intracellular free Ca^{2+} and free arachidonate through pathways that are only partially PKC-dependent. Rapidly induces tyrosine phosphorylation of focal adhesion kinase ($p125^{FAK}$) and paxillin and causes a rapid and transient activation of MAP kinase in Swiss/3T3 cells. *Purity:≥98% by TLC.* M.W.464.6	10 mg	

Proteins/Enzymes

Product	Cat. No.	Comments	Size	Price
Cholesterol Esterase, Microbial	228180	Catalyzes hydrolysis and formation of cholesterol esters, ranging from cholesterol acetate to cholesterol stearate. *Activity:≥70 units/mg dry weight. Specific activity: ≥100 units/mg protein.*	1000 U	
Cholesterol Oxidase, *Nocardia* sp.	228230	Catalyzes the oxidation of cholesterol to cholest-4-ene-3-one. *Activity: ≥10 units/mg dry weight.. Specific activity: >11 units/mg.*	100 IU	
Cholesterol Oxidase, *Streptomyces* sp.	228250	Catalyzes oxidation of cholesterol to cholesterone and hydrogen peroxide. Suitable for determination of total cholesterol when coupled with cholinesterase and peroxidase. Has an optimal pH of 6.0 - 8.0. *Specific activity: ≥40 units/mg.* M.W. 38,000.	500 U	
Lipase, *Chromobacterium viscosum*	437707	Catalyzes hydrolysis of triglycerides to glycerol and fatty acids. *Activity:≥2500 units/mg dry weight.* M.W. 120,000	100 KU	
Phospholipase C, *Bacillus cereus*	525186	Catalyzes the hydrolysis of lecithins to 1,2-diglycerides and choline phosphate. *Activity: ≥50 units/mg dry weight.* M.W. 20,000	250 U	
Phospholipase D, *Streptomyces chromofuscus*	525200	Catalyzes the hydrolysis of lecithin to phosphatidic acid and choline. *Activity:≥50 units/mg dry weight.* M.W. 50,000	250 U	
Phospholipase C-γ-1, His•Tag® fusion	525188	Full-length, recombinant, human phospholipase Cγ-1 expressed in *S. frugiperda* with N-terminal His•Tag® and S•Tag™ sequences. This preparation is qualified for use as a substrate for protein tyrosine kinases in *in vitro* assays. *Purity: >90% by SDS-PAGE.* M.W. 154,300	50 µg	
Phospholipase C-γ-2, His•Tag® fusion, *S. frugiperda*	525189	Full-length, recombinant, human phospholipase C γ-2 expressed in *S. frugiperda* with N-terminal His•Tag® and S•Tag™ sequences. This preparation is qualified for use as a substrate for protein tyrosine kinases in *in vitro* assays. *Purity: >90% by SDS-PAGE.* M.W. 153,600	50 µg	
Sphingolipid Ceramide N-Deacylase, *Pseudomonas* sp.	567704	Hydrolyzes the N-acyl linkage between fatty acids and the sphingosine base of ceramide in various sphingolipids and gangliosides. This enzyme can also catalyze the reverse reaction and transacylation. It is not recommended for hydrolysis of ceramide. *Activity: ≥1 unit/ml.* M.W. 52,000	250 mU	
Sphingomyelinase, *staphyloccus aureus*	567707	Catalyzes the hydrolysis of sphingomyelin to ceramide and phosphocholine. *Specific activity: ≥100 units/mg protein.*	10 U	

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Lipids in Diabetes and Obesity

Antibodies to Phospholipases

Product	Cat. No.	Comments	Size	Price
Anti-Phospholipase A_2, Type VI (557-576) Rabbit pAb	525162	Polyclonal IgG, undiluted serum. Immunogen: a synthetic peptide corresponding to amino acids 557-576 of CHO cell-derived iPLA2, conjugated to KLH. Recognizes the ~80-85 kDa (doublet) iPLA2 protein. Reacts with hamster, human, mouse. **IB**	200 µl	
PhosphoDetect™ Anti-Phospholipase Cγ1 (pTyr^{783}) Rabbit pAb	ST1020	Polyclonal IgG, purified. Immunogen: a synthetic phosphopeptide corresponding to amino acids surrounding the Tyr^{783} phosphorylation site of human PLCg1. Recognizes the ~135 kDa PLCg1 protein phosphorylated at Tyr^{783} in NIH3T3 cells treated with PDGF. Reacts with bovine, human, mouse, rat, *Xenopus*. **IB, IC**	10 T	

IB: immunoblotting; **IC**: immunocytochemistry; **pAb**: polyclonal

Lipase and Phospholipase Inhibitors

Product	Cat. No.	Comments	Size	Price
Lipase Inhibitor, THL	437701	A cell-permeable, reactive, β-lactone compound that acts as a tight-binding, irreversible inhibitor of gastric and pancreatic lipases. *Purity:≥97% by HPLC.* M.W. 495.7	50 mg	
Monoacylglycerol Lipase Inhibitor, URB602	475740	A cell-permeable N-biphenyl carbamate compound that acts as a selective and non-competitive inhibitor of monoacylglycerol lipase (IC_{50} = 28 µM for rat brain MGL). *Purity:≥98% by HPLC.* M.W. 295.4	10 mg	
RHC-80267	554994	Selective inhibitor of DAG lipase activity in (IC_{50} = 4 nM in canine platelets). Also inhibits glucose- and carbachol-induced insulin release from intact islets. *Purity:≥98% by TLC.* M.W. 394.6	10 mg	
$AACOCF_3$	100109	A cell-permeable trifluoromethyl ketone analog of arachidonic acid. Potent and selective slow-binding inhibitor of human cytosolic (85 kDa) PLA_2. Causes a significant reduction in thromboxane B_2 production in thrombin-stimulated platelets.	10 mg	
ACA	104550	Inhibits epinephrine-stimulated thromboxane production (86% at 3.5 µM) via inhibition of PLA2 in human platelets. Possesses moderate leukotriene antagonist activity. *Purity:≥99% by TLC.* M.W. 337.4	25 mg	
Aristolochic Acid	182300	A 1:1 mixture of aristolochic acids I and II. Inhibits PLA_2 from various snake venoms as well as human platelet and synovial fluid PLA_2. Also inhibits ionophore-stimulated PLA2 activity (IC_{50} = 40 µM) and Ca^{2+}-dependent arachidonic acid released in human neutrophils. Exhibits greater inhibitory activity towards group II PLA_2 versus group I PLA_2. *Purity:≥97% by TLC.* M.W. 341.3	50 mg	
D609, Potassium Salt	251400	Selective inhibitor of phosphatidylcholine-specific phospholipase C (*Bacillus cereus*, K_i = 5–10 µM). Does not inhibit (up to 50 µM) phosphatidylinositolspecific phospholipase C, PLA2, and PLD. Also inhibits the activity of sphingomyelinase. *Purity:≥97% by TLC.* M.W. 266.5	5 mg	
ET-18-OCH_3	341207	A selective inhibitor of phosphatidylinositol-specific PLC (IC_{50} = 15 µM) but has no significant effect on phosphatidylcholine-specific PLC or PLD. *Purity:≥95% by TLC.* M.W. 523.7	5 mg	
Isotetrandrine	419650	A biscoclaurine alkaloid that inhibits G-protein activation of phospholipase A_2 but not phospholipase C or phospholipase D. *Purity:≥98% by TLC.* M.W. 622.8	1 mg	
Methyl Arachidonyl Fluorophosphonate	454565	A selective, active site-directed, irreversible inhibitor of both calcium-dependent and calcium-independent cytosolic (85 kDa) PLA_2, but not secretory PLA_2. *Purity:≥98% by TLC.* M.W. 370.5	1 mg	
MJ33	475865	A novel, active-site directed, specific, competitive, and reversible inhibitor of PLA_2. Shows high specificity for type I (pancreatic) and bee venom PLA_2, but has relatively poor affinity for the type II human synovial PLA_2. MJ33 has shown inhibitory activity against a low pH calcium-independent enzyme, as well as against the PLA_2 activity, which is responsible for permeability barrier homeostasis or esophagitis. *Purity:≥90% by ^{31}P-NMR.* M.W. 498.5	5 mg	
Neomycin Sulfate	4801	An inhibitor of inositol phospholipid turnover. A non-specific PLC inhibitor. Also inhibits phophatidylcholine-PLD activity (IC_{50} = 65 µM). M.W. 908.9	25 g	

Lipase and Phospholipase Inhibitors *(continued)*

Product	Cat. No.	Comments	Size	Price
Neomycin Sulfate, γ-Irradiated, Tissue Culture Grade	480100	An inhibitor of inositol phospholipid turnover. A non-specific PLC inhibitor. Also inhibits phophatidylcholine-PLD activity (IC_{50} = 65 mM). M.W. 908.9	20 ml	
$PACOCF_3$	506274	A novel Ca^{2+}-independent PLA2 inhibitor (IC_{50} = 3.8 µM). May also inhibit Ca^{2+}-dependent PLA_2 at higher concentrations (IC_{50} = 45 µM). *Purity:≥97% by TLC.* M.W. 308.4	5 mg	
cPLA2α Inhibitor	525143	A cell-permeable, highly specific, potent inhibitor of cytosolic PLA2α (IC_{50} = 1.8 nM). Exhibits ~230-fold greater potency in enzyme assays and ~3900-fold greater potency in cellular assays compared to $AACOCF_3$ (Cat. No. 100109). M.W. 840.0	500 µg	
$sPLA_2$-IIA Inhibitor I	525145	A highly hydrophobic cyclic pentapeptide that selectively binds and acts as a potent inhibitor of human type IIA secreted PLA2 (IC_{50} = 12.8 µM). Reported to effectively block $sPLA_2$-IIA-induced PGE_2 production at 100 nM in human rheumatoid synoviocytes and is non-toxic at doses up to 10 µM. Does not affect the activities of porcine $sPLA_2$-IB, *Naja naja* $sPLA_2$-IB, or *Crotalus durissus* $sPLA_2$-IIA even at 10 µM. *Purity:≥95% by HPLC.* M.W. 864.9	1 mg	
Quercetin, Dihydrate	551600	An inhibitor of PI 3-kinase (IC_{50} = 3.8 mM) and phospholipase A2 (IC_{50} = 2 µM). Also inhibits mitochondrial ATPase, phosphodiesterases, and PKC. *Purity:≥98% by HPLC.* M.W. 338.3	100 mg	
Quinacrine, Dihydrochloride	551850	A phospholipase A_2 inhibitor that also inhibits the activity of monoamine oxidase. *Purity:≥98% by HPLC.* M.W. 472.9	100 mg	
Spermine, Tetrahydrochloride	5677	Polyamine that plays an important role in the regulation of cellular proliferation and differentiation. Acts as an inhibitor of PLC-α and an activator of PLC-δ. *Purity:≥99% by titration.* M.W. 348.3	5 g	
D-*erythro*-Sphingosine, Dihydro-	300230	Biosynthetic precursor of sphingosine. Inhibits PKC in Chinese hamster ovary cells (IC_{50} = 2.9 µM). *Purity:≥98% by TLC.* M.W. 301.5	10 mg	
ST638	567790	A protein tyrosine kinase inhibitor (IC_{50} = 370 nM) that also inhibits PLD activity in human neutrophils. *Purity:≥98% by HPLC.* M.W. 354.4	5 mg	
U-73122	662035	Inhibits agonist-induced PLC activation (IC_{50} = 1.0–2.1 µM) in human platelets and neutrophils. *Purity:≥99% by TLC.* M.W. 464.7	5 mg	
U-73343	662041	Analog of U-73122 (Cat. No. 662035) that acts as a very weak inhibitor of PLC. Suitable as a negative control. *Purity:≥99% by TLC.* M.W. 466.7	5 mg	

Lipase and Phospholipase Activators

Product	Cat. No.	Comments	Size	Price
Lipoprotein Lipase Activator	437704	A cell-permeable benzylphosphonate derivative that selectively induces lipoprotein lipase (LPL) mRNA and protein levels. *Purity:≥95% by HPLC.* M.W. 451.3	5 mg	
Phospholipase C Activator, *m*-3M3FBS	525185	A cell-permeable and specific activator of phospholipase C (PLC). Activates all PLC isotypes (β2, β3, γ1, γ2, and δ1) *in vitro*, but not heterotrimeric G proteins, PI 3-kinase, or PLD. *Purity:≥95% by HPLC.* M.W. 343.4	10 mg	

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Lipids in Diabetes and Obesity

Fatty Acid Hydrolase/Fatty Acid Synthase Inhibitors

Product	Cat. No.	Comments	Size	Price
FAAH Inhibitor I	341248	A cell-permeable carbamate compound that acts as a potent, selective, and irreversible inhibitor of fatty acid amide hydrolase (FAAH; IC_{50} = 396 nM in brain membranes). Shown to block anandamide (Cat. No. 172100) breakdown in cultured rat cortical neurons (IC_{50} = 214 nM) and inhibit brain FAAH activity (ID_{50} = 0.6 mg/kg) and modulate anxiety in rats. *Purity:≥95% by HPLC.* M.W. 299.4	10 mg	
FAAH Inhibitor II	341249	A cell-permeable carbamate compound that acts as a potent, selective, and irreversible inhibitor of fatty acid amide hydrolase (FAAH; IC_{50} = 4.6 nM in brain membranes). Shown to block anandamide (Cat. No. 172100) breakdown in rat cortical neurons (IC_{50} = 500 pM) and modulate anxiety in rats (ID_{50} = 0.15 mg/Kg). *Purity:≥97% by HPLC.* M.W. 338.4	5 mg	
Fatty Acid Synthase Inhibitor, C75	341325	A cell-permeable α-methylene-γ-butyrolactone compound that potently inhibits FAS (fatty acid synthase) activity and stimulates CPT-1 (carnitine palmitoyltransferase-1), two key enzymes involved in the fatty acid biosynthesis. Acts centrally (reduces NPY expression) and peripherally (activates CPT-1 and fatty acid oxidation activity) to cause reduced food intake and body weight in mice. Promotes cell cycle arrest in human cancer cells culminating in apoptosis. *Purity:≥95% by HPLC.* M.W. 254.3	1 mg 5 mg	
TOFA (5-(Tetradecyloxy)-2-furoic acid)	613450	A cell-permeable furoic acid compound that acts as a potent, reversible, and competitive inhibitor of acetyl-CoA carboxylase (ACC), a key enzyme involved in the fatty acid biosynthesis. Inhibits cellular fatty acid synthesis in a dose-dependent manner (IC_{50} = 4 µM in human breast cancer cell line MCF7). TOFA-induced reduction in malonyl-CoA is reported to off-set the effect of C75 (Cat. No. 341325) on food intake in fasted mice and on apoptosis in tumor cells. *Purity:≥98% by HPLC.* M.W. 324.5	5 mg	

Sphingomyelinase Inhibitors

Ceramide, a sphingosine-based lipid-signaling molecule, has gained serious attention as an important signaling molecule in cell cycle, cell differentiation, apoptosis, and immune response. Ceramide is generated either through *de novo* synthesis mediated by ceramide synthase or through hydrolysis of membrane sphingomyelin by an acid or neutral sphingomyelinase. Acid and neutral sphingomelinases differ in their ion dependence, pH optima, and cellular localization. Recent evidence suggests that the activation of a non-specific lipid scramblase during apoptosis induces the flipping of sphingomyelin from the cell surface to the cytoplasm side of the plasma membrane where it is cleaved by neutral sphingomyelinase to generate ceramide. The production of ceramide induces blebbing of the plasma membrane and aids in rapid engulfment by phagocytes. Neutral sphingomyelinase-released ceramide has also been shown to be essential for capping of L-selectin in lymphocytes.

Some evidence exists indicating that acid sphingomyelinase deficient cells have defects in apoptotic signaling pathways. Sphingomyelin is usually rapidly broken down in the late endosomes and lysosomes. Hence, in acid sphingomyelinase deficiency, sphingomyelin may be kinetically trapped in lysosomes and disrupt endocytic trafficking of raft-associated cell surface signaling molecules. Defects in acid sphingomyelinase have also been linked to lysosomal storage disease known as Niemann-Pick disease, which results in progressive enlargement of liver and spleen.

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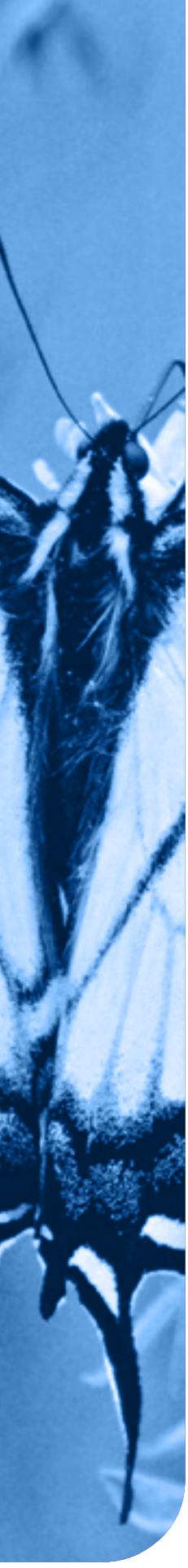
Sphingomyelinase Inhibitors and Stimulators

Product	Cat. No.	Comments	Size	Price
Chlorpromazine, Hydrochloride	215921	An inhibitor of calmodulin-dependent stimulation of cyclic nucleotide phosphodiesterase (IC_{50} = 17 µM) that inhibits lysosomal sphingomyelinase activity. Also acts as a potent PLA2 inhibitor. *Purity:≥99% by titration.* M.W. 355.3	500 mg	
3,4-Dichloroisocoumarin	287815	A potent, irreversible inhibitor of serine proteases. Blocks the activation of neutral sphingomyelinase. *Purity: >99% by elemental analysis. Purity:≥99% by elemental analysis.* M.W. 215	10 mg	
Fumonisin B_1, *Fusarium moniliforme*	344850	A cell-permeable mycotoxin that is acts as a specific inhibitor of ceramide synthase (IC_{50} = 100 nM), but enhances the activity of acidic sphingomyelinase. *Purity:≥98% by TLC.* M.W. 721.8	1 mg	
Gentamycin Sulfate	345814	A broad-spectrum antibiotic that reduces sphingomyelinase activity in fibroblasts. M.W. 463	1 g	
Manumycin A, *Streptomyces parvulus*	444170	An antibiotic that acts as an inhibitor of neutral sphingomyelinase. *Purity:≥ 96% by HPLC.* M.W. 550.7	1 mg	
N-SMase Inhibitor, GW4869	567715	A cell-permeable, potent, specific, non-competitive inhibitor of N-SMase (neutral sphingomyelinase) [IC_{50} ~1 µM, rat brain; Km for sphingomyelin ~13 µM]. Does not inhibit human A-SMase (acid sphingomyelinase) even at 150 µM. *Purity≥90% by HPLC.* M.W. 577.5.	1 mg	
N^{α}-Tosyl-Phe Chloromethyl Ketone (TPCK)	616387	An irreversible inhibitor of chymotrypsin that blocks the activation of neutral sphingomyelinase. *Purity:≥98% by TLC.* M.W. 351.5	250 mg 1 g	



HMG-CoA Reductase Inhibitors and Other Hypocholesterolemic Agents

HMG-CoA reductase catalyzes the 4-electron reduction of HMG-CoA to CoA and mevalonate, with oxidation of two molecules of NADPH. Regulation of the expression of hepatic HMG-CoA reductase is critical in maintaining normal cholesterol levels in serum and tissues. HMG-CoA reductase inhibitors (statins) are competitive inhibitors of this enzyme and have hypocholesterolemic properties. These inhibitors have close resemblance to HMG-CoA. During cholesterol biosynthesis they competitively inhibit the conversion of HMG-CoA to mevalonate, thereby reducing cholesterol biosynthesis in hepatic cells. This results in the enhanced synthesis of LDL-C receptors and increased uptake of LDL-C particles, which enhances cholesterol clearance from the plasma. Ultimately, LDL-C and total cholesterol concentrations are reduced.

HMG-CoA reductase inhibitors differ in their pharmacokinetic properties and drug interaction profiles. For example, Lovastatin and Simvastatin are extensively metabolized by CYP3A4, an isozyme of the P450 system, and thus have the potential to interact with other drugs competing for or inhibiting this isoform. Both Lovastatin and Simvastatin are prodrugs in the lactone form and must be converted to active metabolites by the liver. On the other hand, pravastatin is not extensively metabolized by the P450 system. It is administered in its active hydroxyl acid form and is more hydrophilic and less protein-bound.

Inhibitors

Product	Cat. No.	Comments	Size	Price
Cerulenin, *Cephalosporium caerulens*	219557	An antifungal antibiotic that inhibits sterol and fatty acid biosynthesis. In fatty acid synthesis, reported to bind in equimolar ratio to β-keto-acyl-ACP synthase. In sterol synthesis, inhibits HMG-CoA synthetase activity. *Purity:≥98% by TLC.* M.W. 223.3	5 mg	
Fluvastatin, Sodium Salt	344095	A synthetic HMG-CoA reductase inhibitor (IC_{50} = 40–100 nM for human liver microsomes) that acts as anti-hypercholesterolemic agent. *Purity:≥98% by HPLC.* M.W. 433.4	25 mg	
Lovastatin	438185	An anti-hypercholesterolemic agent that inhibits the activity of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase. (IC_{50} = 27 nM). *Purity:≥95% by HPLC.* M.W 404.5	25 mg	
Lovastatin, Sodium Salt	438186	Carboxylate form of Lovastatin (Cat. No. 438185) that is active in whole cells and cell-free assays. (IC_{50} = 27 nM). *Purity:≥95% by HPLC.* M.W. 444.5	5 mg	
LY 295427	440209	A novel hypocholesterolemic agent that reduces plasma cholesterol levels in animals by increasing the expression of hepatic low-density lipoprotein (LDL) receptors. However, recent studies have attributed the hypocholesterolemic activity of LY 295427 to its ability to reverse oxysterol-mediated suppression of sterol regulatory element-binding protein (SREBP) processing. Micromolar concentrations of this sterol restored the metabolism of LDL in oxysterol-treated cultured cells and inhibited the stimulation of cholesteryl ester synthesis mediated by oxysterols. *Purity:≥95% by TLC.* M.W. 428.7	5 mg	
Mevastatin	474700	An antibiotic that acts as a potent inhibitor of HMG-CoA reductase, thus suppressing Ras farnesylation. *Purity:≥95% by HPLC.* M.W. 390.5	50 mg	
Mevastatin, Sodium Salt	474705	Carboxylate form of Mevastatin (Cat. No. 474700) that is active in whole cells and in cell-free assays. *Purity:≥98% by TLC.* M.W. 430.5	5 mg	
Pravastatin, Sodium Salt	524403	A water-soluble, competitive inhibitor of HMG-CoA reductase (IC_{50} = 95 nM) that potently blocks *in vivo* cholesterol synthesis. *Purity:≥98% by HPLC* M.W. 446.5	25 mg	
Simvastatin	567020	A lipophilic HMG-CoA reductase inhibitor (IC_{50} = 18 nM) that blocks Ras function through inhibition of farnesylation. *Purity:≥98% by HPLC.* M.W. 418.6	50 mg	
Simvastatin, Sodium Salt	567021	Carboxylate form of Simvastatin (Cat. No. 567020) that is active in whole cells and in cell-free preparations. *Purity:≥95% by HPLC.* M.W. 458.6	5 mg	

Peroxisome Proliferator-Activated Receptors (PPARs)

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, γ, and δ 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 (TZDs), 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. In the cell, PPAR forms a heterodimer with the retinoid X receptor (RXR). When induced by TZDs, a conformational change occurs in the heterodimer and co-repressor complexes are displaced. This promotes binding of the PPAR-RXR complex to specific DNA sequences, PPRE, located in the regulatory regions of target 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 glucose transporter GLUT4.

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PPAR

PPAR Agonists

Product	Cat. No.	Comments	Size	Price
Ciglitazone	230950	A potent thiazolinedione type anti-hyperglycemic agent and a selective PPARγ agonist (EC_{50} = 3 µM). *Purity:≥98% by TLC.* M.W. 333.5	5 mg	
Clofibrate	231405	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	500 mg	
GW1929	370695	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	1 mg	
GW7647	370698	A cell-permeable, potent, and selective PPARα agonist (PPARα, γ and δ - EC_{50} = 6 nM, 1.1 mM 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	5 mg	
L-165,041	422175	A cell-permeable, potent, and selective peroxisome proliferator activator receptor δ agonist (K_i = 6 nM for hPPARδ and 730 nM for hPPARγ). Induces adipocyte differentiation in NIH-PPARδ cells at 500 nM. *Purity: ≥98% by HPLC.* M.W. 402.4	5 mg	
LY 171883	440198	A selective, orally active leukotriene D_4 antagonist (K_i = 630 nM for ^{3}H-LTD_4 binding to guinea pig lung membranes). Activates peroxisome proliferation-activated receptors (PPARs). *Purity:≥98% by TLC.* M.W. 318.4	10 mg	
PPARγ Activator, Fmoc-Leu	344034	An N-protected leucine analog that acts as a selective modulator of peroxisome proliferator-activated receptor γ (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:≥98% by HPLC.* M.W. 353.4	250 mg	
Troglitazone	648469	An α-tocopherol moiety containing thiazolidinedione class of insulin-sensitizer that acts as an activator of PPARγ. Exhibits anti-proliferative and anti-inflammatory properties. *Purity:≥98% by TLC.* M.W. 441.5	5 mg	
WY-14643	681725	A potent PPARα ligand. Inhibits TNF-α induced expression of VCAM-1 in endothelial cells. *Purity:≥98% by HPLC.* M.W. 323.8	50 mg	

PPAR Antagonists

Product	Cat. No.	Comments	Size	Price
GW9662	370700	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	5 mg	
PPARγ Antagonist III, G3335	516566	A cell-permeable dipeptide that acts as a selective and reversible PPARγ antagonist (K_D ~ 8 µM). Shown to inhibit the agonist activity of Rosiglitazone (100 nM) in a dose-dependent manner (IC_{50} = 31.9 µM) in transfected COS-7 cells. *Purity:≥97% by elemental analysis.* M.W. 333.3	50 mg	
T0070907	575305	A cell-permeable, potent, specific, irreversible, and high-affinity antagonist of PPARγ with a K_i of 1 nM. Displays >800-fold greater selectivity for PPARγ over PPARα and PPARδ (K_i = 0.85 µM 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	5 mg	

PPAR Receptors and Antibodies to Receptor Related Proteins

Product	Cat. No.	Comments	Size	Price
PPARα, Human, Recombinant, *E. coli*	516559	PPARα is expressed most in 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 aspects of lipid catabolism 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	10 KU	
Anti-PGC-1, C-Terminal (777-797) Rabbit pAb	516557	Polyclonal IgG, purified. Immunogen: a synthetic peptide [(C)SKYDSLDFDSLLKEAQRSLRR] corresponding to amino acids 777-797 of the human PPARγ Coactivator 1 (PGC-1) protein. Recognizes the ~92-105 kDa (apparent MW) PGC-1 protein. Reacts with human and mouse. **ELISA, IB, IH**	100 µl	

ELISA: enzyme-linked immunosorbent assay; **IB**: immunoblotting; **IH**: immunohistochemistry; **pAb**: polyclonal

Phosphodiesterases

cAMP and cGMP, two important second messengers molecules are hydrolyzed by phosphodiesterases (PDEs) in the cell, leading to cessation of cAMP and cGMP-dependent effects. PDEs comprise a large group of enzymes organized into 11 distinct families based on their biochemical and molecular properties. Many of these isozymes are differently 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 complications, erectile dysfunctions, PDEs are considered to be attractive targets for pharmacological intervention. Erectile dysfunction is a common multi-factorial complication of diabetes mellitus and PDE V inhibitor therapy has been found to be effective in special clinical populations, such as those with prostate cancer, diabetes, and cardiovascular disease.

Antibodies

Product	Cat. No.	Comments	Size	Price
Anti-Phosphodiesterase V Rabbit pAb	524583	Polyclonal IgG, serum diluted in PBS. Immunogen: cGMP-binding, cGMP-specific PDE (PDE V, cGB-PDE) purified from bovine lung. Recognizes the PDE V protein. Reacts with bovine. **IB, IP**	50 µl	

IB: immunoblotting; **IP**: immunoprecipitation; **pAb**: polyclonal

Phosphodiesterases

Product	Cat. No.	Comments	Size	Price
Phosphodiesterase 1A3, Active, Human, Recombinant, *S. frugiperda*	524740	A full-length, human recombinant phosphodiesterdase 1A3. Supplied as a partially purified preparation of catalytically active enzyme. *Activity:≥ 0.5 units/µl. One unit is defined as the amount of enzyme that will convert 1 µmol cAMP to AMP per min at 30°C, pH 7.5.*	10 U	
Phosphodiesterase 3A1, Catalytic Domain, Human, Recombinant, *S. frugiperda*	534736	The catalytically active human Phosphodiesterase 3A1, catalytic domain is expressed in *Spodoptera frugiperda. Activity:≥0.5 units/µl. One unit is defined as the amount of enzyme that will convert 1 µmole cAMP to AMP per min at pH 7.5, 30°C.*	10 U	
Phosphodiesterase 3B, Active, Human, Recombinant, *S. frugiperda*	524734	Full-length catalytically active human Phosphodiesterase 3B expressed in *Spodoptera frugiperda. Activity:≥0.5 units/µl. One unit is defined as the amount of enzyme that will convert 1 µmole cAMP to AMP per min at pH 7.5, 30°C.*	10 U	
Phosphodiesterase 4A4, Active, Human, Recombinant, *S. frugiperda*	524731	The full-length catalytically active human Phosphodiesterase 4A4 expressed in *Spodoptera frugiperda. Activity:≥0.5 units/µl. One unit is defined as the amount of enzyme that will convert 1 µmole cAMP to AMP per min at 30°C, pH 7.5.*	10 U	
Phosphodiesterase 4B2, Catalytic Domain, His•Tag®, Human, Recombinant, *S. frugiperda*	524732	Catalytically active human phosphodiesterase catalytic domain expressed in *Spodoptera frugiperda. Activity:≥0.5 units/µl. One unit is defined as the amount of enzyme that will convert 1 µmole cAMP to AMP per min at pH 7.5, 30°C.*	10 U	

Phosphodiesterases

Phosphodiesterases *(continued)*

Product	Cat. No.	Comments	Size	Price
Phosphodiesterase 4B2, Active, Human, Recombinant, *S. frugiperda*	524736	Full-length, recombinant, human phosphodiesterase 4B2 (PDE4B2) expressed in *Spodoptera frugiperda* using a baculovirus expression system. Supplied as a partially purified, catalytically active preparation. *Activity:≥ 0.5 units/µl. One unit is defined as the amount of enzyme that will convert 1 µmol cAMP to AMP per min at 30°C, pH 7.5.*	10 U	
Phosphodiesterase 4C2, Active, Human, Recombinant, *S. frugiperda*	524737	Full-length, human recombinant phosphodiesterdase 4C2 expressed in *Spodoptera frugiperda* using a baculovirus expression system. Supplied as a partially purified preparation of catalytically active enzyme. *Activity:≥ 0.5 units/µl. One unit is defined as the amount of enzyme that will convert 1 µmol cAMP to AMP per min at 30°C, pH 7.5.*	10 U	
Phosphodiesterase 4D3, Active, Human, Recombinant, *S. frugiperda*	524733	Full-length catalytically active human phosphodiesterase 4D3 expressed in *Spodoptera frugiperda. Activity:≥0.5 units/µl. One unit is defined as the amount of enzyme that will convert 1 µmole cAMP to AMP per min at pH 7.5, 30°C.*	10 U	
Phosphodiesterase, Type II, Calf Spleen	524711	Useful in sequence studies of oligonucleotides derived from RNA and DNA. Attacks the 5'-terminal end of phosphodiester bonds, releasing 3'-mononucleotides.	10 U	
Phosphodiesterase 5, Catalytic Domain, Human, Recombinant, *S. frugiperda*	524738	Recombinant, human phosphodiesterase 5 catalytic subunit expressed in *Spodoptera frugiperda* using a baculovirus expression system. Supplied as a partially purified, catalytically active preparation. *Activity:≥ 0.5 units/µl. One unit is defined as the amount of enzyme that will convert 1 µmol cGMP to GMP per min at 30°C, pH 7.5.*	10 U	
Phosphodiesterase, Type V, cGMP-Specific, Bovine, Recombinant, *Spodoptera frugiperda*	524715	Partially purified, catalytically active, dimeric holoenzyme. A target enzyme for Viagra (sildenafil). Suitable for enzymatic studies and as a standard in Western blots using Anti-Phosphodiesterase V Antibody (Cat. No. 524583).	50 µl	
Phosphodiesterase 11A1, Active, Human, Recombinant, *S. frugiperda*	524735	The full-length catalytically active human PDE11A1 expressed in *Spodoptera frugiperda. Activity:≥0.5 units/µl. One unit is defined as the amount of enzyme that will convert 1 µmole cAMP to AMP per min at pH 7.5, 30°C.*	10 U	

Phosphodiesterase V Inhibitors

Product	Cat. No.	Comments	Size	Price
Dipyridamole	322328	A cell-permeable, selective inhibitor of PDE V (IC_{50} = 900 nM). A potent ectonucleosidase inhibitor that also blocks nucleoside transport into mammalian cells. *Purity:≥99% by TLC.* M.W. 504.6	100 mg	
3-Isobutyl-1-methylxanthine	410957	A cell-permeable, non-specific inhibitor of cAMP and cGMP phosphodiesterases (IC_{50} = 2–50 µM). Also acts as an adenosine receptor antagonist. *Purity:≥98% by TLC.* M.W. 222.2	250 mg 1 g	
4-{[3',4'-(Methylenedioxy)benzyl]amino}-6-methoxyquinazoline	475250	A potent and specific inhibitor of PDE V (IC_{50} = 230 nM). Elevates the intracellular cGMP level without causing any change in the cAMP level in isolated porcine coronary arteries. Has no effect on other PDE isozymes. *Purity:≥98% by TLC.* M.W. 309.3	1 mg	
MY-5445	474925	A cell-permeable, selective inhibitor of cGMP-specific phosphodiesterase (PDE V; IC_{50} = 600 nM). *Purity:≥98% by TLC.* M.W. 331.8	10 mg	
Phosphodiesterase V Inhibitor II	524714	A cell-permeable, potent, and highly selective phosphodiesterase V inhibitor (IC_{50} = 5 nM for bovine aorta PDE V; IC_{50} >10 µM for human recombinant PDE I & III, and for bovine aorta PDE II & IV). *Purity:≥97% by HPLC.* M.W. 403.5	5 mg	
Zaprinast	684500	A selective inhibitor of PDE V (IC_{50} = 450 nM). *Purity:≥98% by TLC.* M.W. 271.3	25 mg	

Phosphodiesterase Substrates

Product	Cat. No.	Comments	Size	Price
Adenosine 3',5'-cyclic Monophosphate, 2'-O-(N-Methylanthraniloyl)-, Sodium Salt	116806	A fluorescent, cell-permeable analog of cAMP. Suitable as a substrate for phosphodiesterase studies. *Purity:≥98% by HPLC.* M.W. 484.3. *Excitation max.: ~350 nm, Emission max.: ~445 nm*	10 µmol (4.84 mg)	
Guanosine 3',5'-cyclic Monophosphate, 2'-O-(N-Methylanthraniloyl)-, Sodium Salt	370668	A fluorescent, cell-permeable analog of cGMP. Suitable as a substrate for phosphodiesterase studies. *Purity:≥98% by HPLC.* M.W. 500.3. *Excitation max.: ~350 nm, Emission max.: ~441 nm*	10 µmol (5 mg)	

Glucose Transporters

Glucose transport in mammalian cells is dependent upon membrane-associated carrier proteins. Mammalian cells possess two types of glucose carriers (a) the Na^+-glucose co-transporter and the (b) facilitative glucose transporter. The Na^+-glucose co-transporter transports glucose against its concentration gradient by coupling its uptake with the uptake of Na^+. It is largely expressed in epithelial cells of the small intestine and in kidney. The facilitative glucose carriers of the glucose transporters (GLUT) family accelerate the transport of glucose down its concentration gradient by facilitative diffusion. Members of the GLUT family are expressed in a tissue- and cell-specific manner and exhibit distinct kinetic and regulatory properties that reflect their specific functional roles.

GLUT1 is a widely expressed isoform that provides cells with their basal glucose requirements. It plays a unique role in transporting glucose across epithelial and endothelial barrier tissues. GLUT2 is a high K_m isoform expressed in hepatocytes, pancreatic β-cells, and the basolateral membranes of intestinal and renal epithelial cells. It acts as a high-capacity transport system to allow the flux of glucose into or out of these cells in a non-rate-limiting manner. In the liver GLUT2 mediates the bi-directional transport of glucose by hepatocytes. GLUT3 is a low K_m isoform that is responsible for glucose uptake into neurons. The localization of the GLUT4, mainly expressed in insulin sensitive tissues, such as muscle and adipose tissue, changes in response to insulin. It is responsible for increased glucose disposal in these tissues in the postprandial state and is vital in whole-body glucose homeostasis. The GLUT5, expressed in small intestine is involved in the trans-cellular transport of glucose by absorptive epithelial cells. GLUT7 is present in the endoplasmic reticulum (ER) membrane that allows the flux of free glucose out of the lumen of ER following the action of glucose-6-phosphatase on glucose 6-phosphate. GLUT6 and GLUT8 appear to recycle in a dynamin-dependent manner between internal membranes and the plasma membrane in rat adipose cells.

It is clear that each glucose transporter operates most efficiently at different levels of blood glucose. For example, GLUT4 can swiftly reduce high levels of glucose in the post-parandial state. Elevated cell surface levels of the GLUT4 facilitate enhanced glucose uptake from the circulation and storage in fat and muscle. GLUT3 operates efficiently at low blood glucose concentrations in order to ensure constant supply of glucose to the brain when blood glucose levels are low. GLUT2, in its regulatory function, has an activity that is linear across a wide range of blood glucose concentrations and can provide an insulin demand signal to the pancreatic β-cells at various glucose levels.

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Glucose Transporters

Antibodies

Product	Cat. No.	Comments	Size	Price
Anti-Glucose Transporter-1 Rabbit pAb	400060	Polyclonal IgG, purified. Immunogen: a synthetic peptide corresponding to amino acids near the C-terminus of mouse Glut-1, conjugated to KLH. Recognizes the ~42-45 kDa Glut-1 protein. Also recognizes the Hep G2-type transporter. Reacts with human, mouse, rabbit, rat. **ELISA, FS, IB, IF, IP**	50 µg	
Anti-Glucose Transporter-2 Rabbit pAb	400061	Polyclonal IgG, purified. Immunogen: a synthetic peptide corresponding to amino acids in the cytoplasmic domain of rat Glut-2, conjugated to KLH. Recognizes the ~53-61 kDa Glut-2 protein. Reacts with human, mouse, rat. **ELISA, IB**	50 µg	
Anti-Glucose Transporter-3 Rabbit pAb	400062	Polyclonal IgG, purified. Immunogen: a synthetic peptide corresponding to amino acids near the C-terminus of human Glut-3, conjugated to KLH. Recognizes the ~45 kDa Glut-3 protein. Reacts with human. **ELISA, FS, IB, IF, IP**	50 µg	
Anti-Glucose Transporter-4 Rabbit pAb	400064	Polyclonal IgG, purified. Immunogen: a synthetic peptide corresponding to amino acids near the C-terminus of mouse Glut-4, conjugated to KLH. Recognizes the ~40-43 kDa Glut-4 protein. Reacts with human, mouse, rat. **ELISA, FS, IB, IP**	50 µg	
Anti-Glucose Transporter-5 Rabbit pAb	400066	Polyclonal IgG, purified. Immunogen: a synthetic peptide corresponding to amino acids from the cytoplasmic region of rat Glut-5, conjugated to KLH. Recognizes the ~60 kDa Glut-5 protein. Also recognizes a ~42 kDa protein in rat kidney. Reacts with rat. **ELISA, FS, IB, IF**	50 µg	

ELISA: enzyme-linked immunosorbent assay; **FS**: frozen sections; **IB**: immunoblotting; **IF**: immunofluorescence; **IP**: immunoprecipitation; **pAb**: polyclonal

Inhibitors of Glucose Transport

Product	Cat. No.	Comments	Size	Price
Cytochalasin B, Dihydro-	250225	A less potent inhibitor of glucose transport, but exhibits binding affinity (K_d ≈10 nM) similar to cytochalasin B (Cat. No. 250233) in IL-3 dependent mast cell line. *Purity:≥98% by TLC.* M.W. 481.6	1 mg	
Cytochalasin B, *Helminthosporium dematioideum*	250233	Cell-permeable fungal toxin. Inhibits cytoplasmic division by blocking the formation of contractile microfilaments. A non-competitive inhibitor of Glut-1 transport system. Also blocks the transport of deoxyglucose and other substrates by Glut-2 and Glut-3 in *xenopus* oocytes. *Purity:≥98% by HPLC.* M.W. 479.6	5 mg	
Phloretin	524488	A competitive inhibitor of glucose transporter Glut-1. *Purity:≥98% by TLC.* M.W. 274.3	200 mg	

Antibodies to Insulin, IGF, their Receptors and IGF-Binding Proteins

Product	Cat. No.	Comments	Size	Price
Anti-IGF-I (Ab-2) Goat pAb	PC195L	Polyclonal IgG, purified. Immunogen: recombinant human IGF-I. Recognizes human IGF-I. **ELISA, IB, NT**	100 µg	
Anti-IGF-I Receptor (Ab-1) Mouse mAb (αIR3)	GR11T	Monoclonal IgG_1, purified. Immunogen: partially purified IGF-IR receptor from human placenta. Recognizes the ~130 kDa α- and ~90 kDa β-subunits of IGF-1 receptor. Reacts with human. **IF, IP**	10 µg	
Anti-IGF-I Receptor (Ab-1) Mouse mAb (αIR3)	GR11	Monoclonal IgG_1, purified. Immunogen: partially purified IGF-I receptor from human placenta. Reacts with human. **IF, IP**	100 µg	
Anti-IGF-I Receptor (Ab-1) Mouse mAb (αIR3)	GR11L	Monoclonal IgG_1, purified. Immunogen: partially purified IGF-I receptor from human placenta. Reacts with human. **IF, IP, NT**	100 µg	
Anti-IGF-I Receptor (Ab-3) Mouse mAb (33255.111)	GR31L	Monoclonal IgG_1, purified. Immunogen: recombinant human IGF-I soluble receptor. Reacts with human. **ELISA, IB, NT**	100 µg	
Anti-IGF-I Receptor (Ab-2) Goat pAb	PC196L	Polyclonal IgG, purified. Immunogen: recombinant human IGF-I soluble receptor. Reacts with human. **ELISA, IB, NT, PS**	100 µg	
Anti-IGF-I Receptor (Ab-4) Mouse mAb (24-31)	GR38	Monoclonal IgG_1, purified. Immunogen: IGF-IR/3T3 fibroblasts transfected with human IGF-I receptor. Recognizes the ~130 kDa α-subunit of insulin receptor. Reacts with human, rabbit (weakly). **ELISA, IP**	100 µg	
Anti-IGFBP-3 Mouse mAb (84728.111)	GF60	Monoclonal IgG_{2b}, purified. Immunogen: recombinant human IGFBP-3. Reacts with human. **ELISA, IB, PS**	500 µg	
Anti-Insulin Mouse mAb (E2E3C2)	GF44	Monoclonal IgG_1, purified. Immunogen: the membrane fraction of human retinoblastoma tumor tissue. Recognizes the ~56 kDa human insulin. **PS**	100 µg	
Anti-Insulin Receptor (Ab-1) Mouse mAb (CII 25.3)	GR05	Monoclonal IgG_1, purified. Immunogen: partially purified human placental insulin receptor. Does not react with IGF-1 and IGF-II receptors. Reacts with human, Old World monkeys. **IP**	100 µg	
Anti-Insulin Receptor (Ab-3) Mouse mAb (29B4)	GR07	Monoclonal IgG_1, purified. Immunogen: partially purified human placental insulin receptor. Recognizes the ~95 kDa β-subunit. Also cross-reacts with IGF-1 receptor. Reacts with human, mouse, rat. **IP, NT**	100 µg	
Anti-Insulin Receptor (β-Subunit) Mouse mAb (CT-3)	GR36	Monoclonal IgG_1, purified. Immunogen: a protein containing the C-terminal 100 amino acids of the β-subunit of human insulin receptor fused to GST. Recognizes the ~95 kDa β-subunit of insulin receptor. Reacts with human, mouse, rat. **FS, IB, PS**	100 µg	
PhosphoDetect™ Anti-Insulin Receptor ($pTyr^{972}$) Rabbit pAb	GF1000	Polyclonal IgG, immunoaffinity, purified. Immunogen: a synthetic phosphopeptide surrounding the Tyr^{972} phosphorylation site of human IR. Recognizes the ~95 kDa β-subunit phosphorylated at Tyr^{972}. Reacts with human, mouse. **IB**	10 T	

ELISA: enzyme-linked immunosorbent assay; **FS**: frozen sections; **IB**: immunoblotting; **IC**: immunocytochemistry; **IF**: immunofluorescence; **IP**: immunoprecipitation; **mAb**: monoclonal; **NT**: neutralization; **pAb**: polyclonal; **PS**: paraffin sections

Antibodies to Insulin Receptor Substrates

Product	Cat. No.	Comments	Size	Price
PhosphoDetect™ Anti-IRS ($pTyr^{896}$) Rabbit pAb	PC463	Polyclonal IgG, undiluted serum. Immunogen: a synthetic phosphopeptide corresponding to amino acids 891-902 of human insulin receptor substrate-1 (hIRS-1). Reacts with human. **ELISA, IB**	25 µl	
Anti-IRS-1 Mouse mAb (8-36)	GR45	Monoclonal IgG_1, purified. Immunogen: a synthetic peptide corresponding to amino acids 1221-1235 of rat insulin receptor substrate-1 (IRS-1), conjugated to KLH. Recognizing the ~160-185 kDa IRS-1 protein. Reacts with human, mouse, rat. **IB, IP**	100 µg	
Anti-IRS-1 (900-1235) Rabbit pAb	420292	Polyclonal IgG, undiluted serum. Immunogen: a recombinant protein containing amino acids 900-1235 of rat IRS-1 fused to GST. Recognizes the ~160-185 kDa IRS-1 protein. Reacts with human, mouse, rat. **IB, IP**	100 µl	
PhosphoDetect Anti-IRS-1 ($pSer^{307}$) Rabbit pAb	GF1005	Polyclonal IgG, purified. Immunogen: a synthetic phosphopeptide corresponding to amino acids 301-315 surrounding the Ser^{307} phosphorylation site of mouse IRS-1. Recognizes IRS-1 phosphorylated on Ser^{307}. Reacts with mouse. **IB**	100 µg	
PhosphoDetect Anti-IRS-1 ($pSer^{616}$) Rabbit pAb	GF1001	Polyclonal IgG, purified. Immunogen: a synthetic phosphopeptide surrounding the Ser^{616} phosphorylation site of human IRS-1. Recognizes IRS-1 phosphorylated as Ser^{616} in IRS-1 transfect CHO cells. Reacts with human. **IB**	10 T	
PhosphoDetect Anti-IRS-1 ($pSer^{636}$) Rabbit pAb	GF1007	Polyclonal IgG, immunoaffinity, purified. Immunogen used was a synthetic phosphopeptide corresponding to amino acids 631-646 surrounding the Ser^{636} phosphorylation site of mouse IRS-1. Recognizes IRS-1 phophorylated at Ser^{636} in insulin treated 3T3-LI cells. Reacts with mouse. **IB**	100 µg	

ELISA: enzyme-linked immunosorbent assay; **FS**: frozen sections; **GS**: gel shift; **IB**: immunoblotting; **IC**: immunocytochemistry; **IF**: immunofluorescence; **IH**: immunohistochemistry; **IP**: immunoprecipitation; **mAb**: monoclonal; **NT**: neutralization; **pAb**: polyclonal; **PS**: paraffin sections ; **RIA**: radioimmunoassay

Insulin and Insulin like Growth factors

Antibodies to Insulin Receptor Substrates *(continued)*

Product	Cat. No.	Comments	Size	Price
PhosphoDetect™ Anti-IRS-1 (pTyr^{896}) Rabbit pAb	GF1003	Polyclonal IgG, immunoaffinity, purified. Immunogen: a synthetic phosphopeptide surrounding the Tyr^{896} phosphorylation site of human IRS-1. Recognizes IRS-1 phosphorylated at Tyr^{896}. Reacts with human, rat. **IB**	10 T	
PhosphoDetect Anti-IRS-1 (pTyr^{941}) Rabbit pAb	GF1004	Polyclonal IgG, immunoaffinity, purified. Immunogen: a synthetic phosphopeptide surrounding the Tyr^{941} phosphorylation site of human IRS-1. Recognizes IRS-1 phosphorylated at Tyr^{541}. Reacts with human, rat. **IB**	10 T	
Anti-IRS-2 (1122-1321) Rabbit pAb	420293	Polyclonal IgG, undiluted serum. Immunogen: a GST-fusion protein containing amino acids 1122-1321 of mouse IRS-2. Recognizes the ~180 kDa IRS-2 protein. Reacts with hamster, human, mouse, rat. **IB, IP**	100 µl	
PhosphoDetect Anti-IRS1 (pTyr^{612}) Rabbit pAb	PS1010	Polyclonal IgG, purified. Immunogen: a synthetic phosphopeptide corresponding to amino acids surrounding the Tyr^{612} phosphorylation site of human IRS-1. Recognizes the ~165-180 kDa IRS-1 protein phosphorylated at Tyr612. Reacts with human. **IB**	10 T	

IB: immunoblotting; **IP**: immunoprecipitation; **pAb**: polyclonal

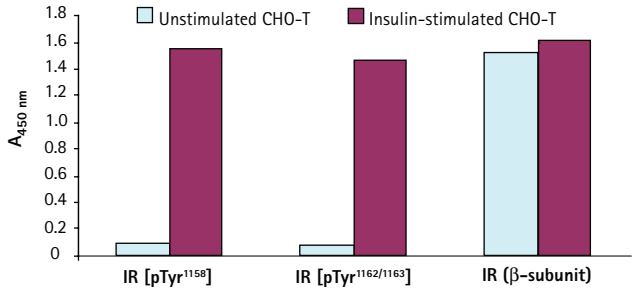
Kits

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 also cross-reacts with mouse and rat cells.

Cat. No. CBA039 **1 kit**



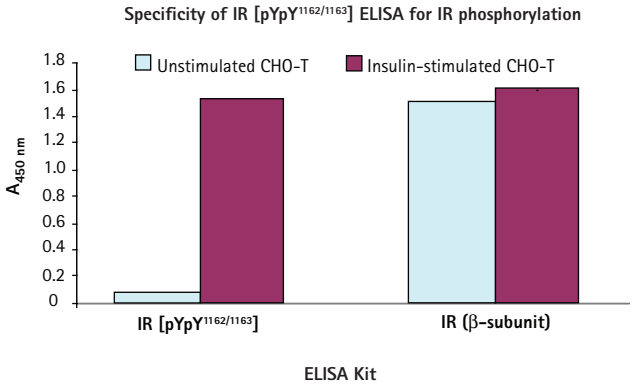
CHO-T cells were stimulated for 10 minutes with 100 nM insulin. Unstimulated cells were used as control. This kit (Cat. No. CBA039) detects phosphorylated IR in stimulated and non-phosphorylated IR in CHO-T cells .

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

Format: 96-well plate
Sensitivity: < 0.8 Units/ml
Assay time: 4 h
Sample type: Cells

Suitable for detection and quantitation of insulin receptor (IR) that is phosphorylated at Tyr$^{1162/1163}$. Although this kit is designed for use with human cell lines, platelets and lymphocytes, it also cross-reacts with mouse and rat cells.

Cat. No. CBA038 **1 kit**



The specificity of this assay for IR phosphorylated at Tyr$^{1162/1163}$ was confirmed by peptide competition. Phosphorylated IR was quantitated in the assay as usual except that the detection antibody was preincubated with IR-derived peptides at a concentration of 0.1-1 µg/ml. The data presented in Figure 3 show that only the peptide corresponding to the region surrounding Tyr$^{1162/1163}$, containing the phospho-tyrosines, could block the ELISA signal. The peptides containing phosphorylated tyrosine at positions 972 and 1158 did not block the signal.

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

Recombinant, human insulin receptor substrate 1 (IRS1) consisting of the p30 fragment (IRS1p30, amino acids 516-777) expressed in *E. coli*. IRS1 is a major endogenous substrate for insulin receptor and IGF-1R tyrosine kinase activity. Although IRS-1 is constitutively phosphorylated on given serine and threonine residues, it is tyrosine-phosphorylated only after stimulation by insulin. This recombinant p30 fragment contains 5 potential tyrosine phosphorylation sites; phosphorylated IRS1p30 will bind to insulin receptor. *Purity: >95% by SDS-PAGE*. M.W. 28,000

Cat. No. 663001 **150 µg**

Selected Hormones, Hormone Receptors, and Hormone Binding Proteins

Product	Cat. No.	Comments	Size	Price
IGFBP-3, Human, Recombinant, NSO Cells	PF135	Contains the mature IGFBP-3 fused to the signal peptide of CD33 and expressed in the mouse myeloma cell line, NSO. IGFBP-3 is a negative regulator of cell growth and proliferation and can be induced by TNF-α and p53. *Biological activity: ED_{50} approximately 0.05-0.15 mg/ml for the inhibition of the biological effect of 14 ng/ml recombinant IGF-II. Purity:≥95% by SDS-PAGE*	25 µg	
Insulin, Zinc, Human, Recombinant, *P. pastoris*	407709	A peptide anabolic hormone produced by pancreatic β-cells. *Activity:≥25 IU/mg (dry basis). Purity:≥95% by HPLC.* M.W. 5807.7	50 mg	
Glucagon, Human	05-23-2700	Peptide hormone secreted by pancreatic α-cells. An important hyperglycemic agent *Purity: >97% by SDS-PAGE.* M.W. 3482.8	0.1 mg 0.5 mg	
Insulin-Like Growth Factor-I, Human, Recombinant, *E. coli*	407240	Has about 40% homology to insulin and produces metabolic effects similar to insulin. Acts as an important local regulator of bone formation. Increases bone formation and bone resorption. Stimulates the activity of protein tyrosine kinases in both normal and diethylstilbestrol-treated hamster kidneys. *Biological activity: ED_{50} = 1.0-3.0 ng/ml as measured in a cell proliferation assay with MCF-7 human breast carcinoma cells. Purity: ≥97% by SDS-PAGE.* M.W. 7500	50 mg	
Insulin-Like Growth Factor-II, Human, Recombinant, *E. coli*	407245	Its actions are similar to IGF-1 (Cat. No. 407240). Plays an important role in fetal development. Stimulates muscle and bone cell proliferation and differentiation. *Biological activity: ED_{50} = 5-10 ng/ml. Purity:≥97% by SDS-PAGE.* M.W. 7500	50 mg	
IGF-1R, GST-Fusion, Human, Recombinant, *S. frugiperda*	325881	Recombinant, human Insulin-like Growth Factor-1 Receptor (IGF-1R) fused at the N-terminus to a GST-His_6-thrombin cleavage site tag and expressed in *S. frugiperda* using a baculovirus expression system. IGF-1R mediates cell survival and growth in response to its ligands, IGF-1 and IGF-2. *Specific activity:≥45 pmol/min/µg protein. Kinase activity is measured as the molar amount of phosphate incorporated into Poly(Glu,Tyr)4:1 per minute per mg protein at 30°C, using variable concentrations from 0.1 µM to 2.52 µM ATP.* M.W. 76,532	10 mg	

Insulin Degrading Enzyme (IDE)

Product	Cat. No.	Comments	Size	Price
Insulin Degrading Enzyme, His•Tag®, Rat, Recombinant, *S. frugiperda*	407241	A metalloprotease that degrades insulin and a variety of other peptides including amyloid peptides. *Specific activity:≥4 U/mg protein. Purity:≥90% by SDS-PAGE.*	50 µg	
Anti-IDE/Insulysin Rabbit pAb	ST1120	Polyclonal IgG, purified. Immunogen: a synthetic peptide corresponding to amino acids at the N-terminus of human IDE/insulysin. Recognizes the ~110 kDa IDE protein in HT1080 cells. Reacts with human. **IB, IP**	50 µg	
Anti-IDE, N-Terminal (97-273) Rabbit pAb	PC730	Polyclonal IgG, undiluted serum. Immunogen: a recombinant protein containing amino acids 97-273 of rat IDE fused to GST. Recognizes the ~115 kDa endogenous and recombinant IDE. Reacts with hamster, human, mouse, rat. **ELISA, IB, IC**	100 µl	

ELISA: enzyme-linked immunosorbent assay; **IB**: immunoblotting; **IC**: immunocytochemistry; **IP**: immunoprecipitation; **pAb**: polyclonal

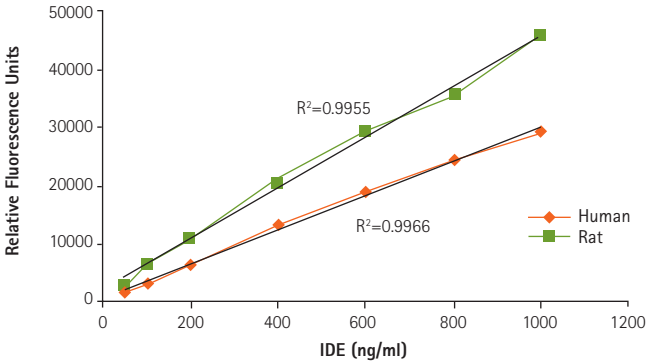
Insulin and Insulin like Growth Factors

Kit

InnoZyme™ Insulysin/IDE Immunocapture Activity Assay Kit

Format: 96-well plate
Detection Method: Fluorescence
Assay range: 50-1000 ng/ml
Assay time: 3.5 h
Sample type: cell lysates, tissue extracts, and biological fluids

A specific and sensitive assay kit for measuring active insulysin (IDE) from human, mouse, or rat samples. This kit employs an affinity-purified polyclonal antibody immobilized on a 96-well plate to capture IDE. Activity of captured IDE is measured using a FRET substrate, Mca-GGFLRKHGQ-EDDnp. Substrate is cleaved between R and K , which releases the fluorophore from the quencher Dnp resulting in increased fluorescence (Exc. 320 nm; Em. 405 nm).



Recombinant rat and human IDE was measured using the InnoZyme™ Insulysin/IDE Immunocapture Activity Assay Kit (Cat. No. CBA079). Incubation period: 4 hours at 37˚C.

Cat. No. CBA079 **1 kit**

Insulin/IGF Receptor Tyrosine Kinases

Inhibitors of Insulin/IGF Receptor Tyrosine Kinases

Product	Cat. No.	Comments	Size	Price
IGF-1R Inhibitor, PPP	407247	A cell-permeable, non-competitive, potent, and specific inhibitor of IGF-1R kinase 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	1 mg	
AG 538	658403	A potent, competitive inhibitor of insulin-like growth factor-1 receptor (IGF-1R) kinase autophosphorylation (IC_{50} = 400 nM). Also inhibits the phosphorylation of PTK substrate poly (Glu,Tyr) by IGF-1R, IR, EGF-R, and Src (IC_{50} = 60 nM, 113 nM, and 2.4 µM respectively). *Purity:≥95% by HPLC.* M.W. 297.3	5 mg	
I-OMe-AG 538	658417	An analog of AG 538 (Cat. No. 658403) that acts as an inhibitor of IGF-1 receptor kinase both *in vitro* and in intact cells. Inhibition is competitive with respect to the substrate binding site of IGF-1 receptor kinase. Exhibits enhanced cell-permeability and increased resistance to oxidation. *Purity:≥95% by HPLC.* M.W. 437.2	5 mg	

Insulin/IGF Receptor Tyrosine Kinases

Inhibitors of Insulin/IGF Receptor Tyrosine Kinases *(continued)*

Product	Cat. No.	Comments	Size	Price
AG 1024	121767	A specific inhibitor of IGF-1 and insulin receptor kinases with significantly lower IC_{50} values for IGF-1 than for insulin receptor kinase. *Purity:≥98% by HPLC.* M.W. 305.2	1 mg	
AGL 2263	121850	A cell-permeable, potent, substrate-competitive, but not ATP-competitive, inhibitor of insulin receptor kinase (IC_{50} = 400 nM) and insulin-like growth factor-1 receptor kinase (IC_{50} = 430 nM). *Purity:≥97% by HPLC.* M.W. 322.3	5 mg	
HNMPA-$(AM)_3$	397100	Cell-permeable inhibitor of insulin receptor tyrosine kinase (IC_{50} = 100 µM). Inhibits insulin-stimulated glucose oxidation in rat adipocytes. *Purity:≥95% by TLC.* M.W. 454.4	5 mg	

β-Insulin Receptor Kinase, GST-Fusion, Human, Recombinant, *S. frugiperda*

GST-fusion protein containing the 48 kDa cytoplasmic domain of the β-subunit of the human insulin receptor, amino acids 941-1343, expressed in a baculovirus expression system. Constitutively active tyrosine kinase. *Specific activity: ≥50 units/mg protein. One unit is defined as the amount of enzyme required to transfer 1 nmol phosphate to poly[Glu: Tyr] 4:1 substrate per min at 25°C. Purity: ≥80% by SDS-PAGE.* M.W. 71,700

Cat. No. 407697 **20 µg**

Insulin Receptor Tyrosine Kinase Activator

Product	Cat. No.	Comments	Size	Price
IRTK Activator	420295	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	5 mg	
IRTK Activator, Negative Control	420296	A negative control compound for IRTK Activator (Cat. No. 420295). *Purity:≥97% by HPLC.* M.W. 322.3	5 mg	

Insulin Mimetics

Product	Cat. No.	Comments	Size	Price
Demethylasterriquinone B1	260010	A cell-permeable, insulin mimic with oral anti-diabetic activity in animal models. 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:≥95% by HPLC.* M.W. 506.6	5 mg	
GSK-3β Peptide Inhibitor, Cell-permeable	361546	A cell-permeable, myristoylated form of GSK-3β Peptide Inhibitor (Cat. No. 361545) with a glycine spacer. Acts as a selective, substrate-specific, competitive inhibitor of GSK-3β (IC_{50} = 40 µM). Shown to mimic insulin action, stimulate glycogen synthase, and improve glucose tolerance in diabetic mice. *Purity:≥98% by HPLC.* M.W. 1464.7	1 mg	

Glucagon Receptor Antagonists

Product	Cat. No.	Comments	Size	Price
Glucagon Receptor Antagonist I	346001	A cell-permeable, potent, selective, and competitive antagonist of the glucagon receptor. Shown to bind to hGCGR with high affinity and prevent 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 human primary hepatocytes and in mice (50 mg/kg, ip). *Purity:≥95% by HPLC.* M.W. 346.5	1 mg 5 mg	
Glucagon Receptor Antagonist, Control	346002	A cell-permeable compound that can be used as an inactive control for Glucagon Receptor Antagonist (Cat. No. 346001). Displays weak affinity to hGCGR. *Purity:≥95% by HPLC.* M.W. 431.4	1 mg 5 mg	
Glucagon Receptor Antagonist II	346003	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+}. Shown to be orally bioavailable in rodent models. *Purity:≥98% by HPLC.* M.W. 467.8	5 mg	

JAK/STAT Pathway products

Antibodies

Product	Cat. No.	Comments	Size	Price
PhosphoDetect™ Anti-JAK2 ($pTyr^{1007/1008}$) Rabbit pAb	PS1014	Polyclonal IgG, purified. Immunogen: a synthetic phosphopeptide corresponding to amino acids surrounding the $Tyr^{1007/1008}$ phosphorylation sites of human JAK2. Recognizes the ~130 kDa JAK2 protein phosphorylated at $Tyr^{1007/1008}$. Reacts with human, mouse, rat. **IB**	100 µl	
PhosphoDetect Anti-JAK1 ($pTyr^{1022/1023}$) Rabbit pAb	420092	Polyclonal IgG, affinity purified. Immunogen: a synthetic phosphopeptide corresponding to amino acids surrounding the Tyr^{1022} and Tyr^{1023} phosphorylation sites of human JAK1 (Janus Kinase 1). Reacts with human, mouse. **IB**	10 T	
Anti-JAK1 Rabbit pAb	PK1004	Polyclonal IgG, purified. Immunogen: a synthetic peptide corresponding to amino acids surrounding $Tyr^{1022/1023}$ of human JAK1, coupled to KLH. Recognizes the ~130 kDa JAK1 protein in CTLL-2 and BaF3 cells. Reacts with human, mouse. **IB, IP, PS**	50 µl	
PhosphoDetect Anti-STAT1 ($pSer^{727}$) Rabbit pAb	569383	Polyclonal IgG, purified. Immunogen: a synthetic phosphopeptide corresponding to amino acids surrounding the Ser^{727} phosphorylation site of human STAT1. Recognizes STAT1 phosphorylated at Ser^{727}. Reacts with human, mouse, and rat. **IB**	10 T	
PhosphoDetect Anti-STAT1 ($pTyr^{701}$) Rabbit pAb	569382	Polyclonal IgG, purified. Immunogen: a synthetic phosphopeptide corresponding to amino acids surrounding the Tyr^{701} phosphorylation site of human STAT1. Recognizes STAT1 phosphorylated at Tyr^{701}. Reacts with human. **IB**	10 T	
Anti-STAT1 Rabbit pAb	569386	Polyclonal IgG, purified. Immunogen: a synthetic peptide corresponding to amino acids surrounding Tyr^{701} of human STAT1. Recognizes the ~90 kDa full-length and the ~84 kDa splice variant of STAT1. Reacts with human, mouse, and rat. **FC, IB, IP**	10 T	
PhosphoDetect Anti-STAT2 ($pTyr^{690}$) Rabbit pAb	ST1106	Polyclonal IgG, purified. Immunogen: a synthetic phosphopeptide corresponding to amino acids surrounding the Tyr^{690} phosphorylation site of human STAT2, coupled to KLH. Recognizes the ~113 kDa human STAT2 protein phosphorylated at Tyr^{690} in HeLa cells. Reacts with human. **IB, IP**	50 µl	
PhosphoDetect Anti-STAT3 ($pTyr^{705}$) Mouse mAb (9E12)	569384	Monoclonal IgG_1, purified. Immunogen: a synthetic phosphopeptide corresponding to amino acids surrounding the Ala-Pro-$pTyr^{705}$-Leu-Lys phosphorylation site of human STAT3. Recognizes STAT3 phosphorylated at Tyr^{705}. Provided with vanadate treated A431 cell lysate as positive control. Reacts with human and mouse. **ELISA, IB, IP**	1 set	
Anti-STAT3 Rabbit pAb	569388	Polyclonal IgG, purified. Immunogen: a synthetic peptide corresponding to amino acids surrounding Tyr^{705} of mouse STAT3. Recognizes native and denatured STAT3. Reacts with human, mouse, and rat. **IB, IC, IP**	100 µl	
PhosphoDetect Anti-STAT5 ($pTyr^{694}$) Rabbit pAb	575142	Polyclonal IgG, purified. Immunogen: a synthetic phosphopeptide corresponding to amino acids surrounding the Tyr^{694} phosphorylation site of mouse STAT5, conjugated to KLH. Recognizes STAT5 phosphorylated at Tyr^{694}. Reacts with human and mouse. **IB, IC**	100 µl	
Anti-STAT5 Rabbit pAb	ST1105	Polyclonal IgG, purified. Immunogen: a synthetic peptide corresponding to amino acids surrounding residue 260 of human STAT5, conjugated to KLH. Recognizes the ~90 kDa STAT5α and STAT5β (doublet) proteins in K562 cells. Reacts with human and mouse. **IB, IP**	50 µl	

ELISA: enzyme-linked immunosorbent assay; **FC**: flow cytometry; **IB**: immunoblotting; **IC**: immunocytochemistry; **IP**: immunoprecipitation; **pAb**: polyclonal; **PS**: paraffin sections

Antibodies *(continued)*

Product	Cat. No.	Comments	Size	Price
PhosphoDetect Anti-STAT6 (pTyr^{641}) Rabbit pAb	575143	Polyclonal IgG, purified. Immunogen: a synthetic phosphopeptide corresponding to amino acids surrounding the Tyr^{641} phosphorylation site of human STAT6, conjugated to KLH. Recognizes the ~94 kDa STAT6 protein phosphorylated at Tyr^{641}. Reacts with human and mouse. **FC, IB, IF**	100 µl	
PhosphoDetect Anti-STAT3 (pTyr^{727}) Rabbit pAb	569392	Polyclonal IgG, purified. Immunogen: a synthetic phosphopeptide corresponding to amino acids surrounding the Ser^{727} phosphorylation site of human STAT3. Recognizes the ~90 kDa STAT3 protein phosphorylated at Ser^{727}. Reacts with human, mouse, rat. **IB**	10 T	

ELISA: enzyme-linked immunosorbent assay; **FC**: flow cytometry; **IB**: immunoblotting; **IC**: immunocytochemistry; **IP**: immunoprecipitation; **pAb**: polyclonal; **PS**: paraffin sections

Enzyme

Product	Cat. No.	Comments	Size	Price
JAK3, GST-Fusion, Human, Recombinant, *S. frugiperda*	325883	Recombinant, human Janus Kinase 3 (JAK3) fused at the N-termiunus to a GST-His$_6$-thrombin cleavage site tag and expressed in *S. frugiperda* using a baculovirus expression system. JAK3 is a member of the Janus family of tyrosine kinases and plays an important role in signal transduction and interacts with members of the STAT (signal transduction and activators of transcription) family. *Specific activity:≥6.0 pmol/min/µg.* M.W. 68,379	10 µg	

Kits

PhosphoDetect™ STAT Antibody Sampler Kit

The kit contains PhosphoDetect™ Anti-STAT1 (pTyr^{701}) Rabbit pAb, PhosphoDetect™ Anti-STAT2 (pTyr^{690}) Rabbit pAb, PhosphoDetect™ Anti-STAT3 (pTyr^{705}) Rabbit pAb, PhosphoDetect™ Anti-STAT3 (pSer^{727}) Rabbit pAb, PhosphoDetect™ Anti-STAT5 (pTyr^{694}) Rabbit pAb (Cat. No. 575142), PhosphoDetect™ Anti-STAT6 (pTyr^{641}) Rabbit pAb (Cat. No. 575143), Goat Anti-Rabbit IgG HRP conjugate, and a data sheet

Cat. No. PS1021 **1 kit**

STAT1 ELISA Kit

Format: 96-well plate
Sensitivity: <0.27 ng/ml
Assay time: 4 h
Sample type: Cells

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

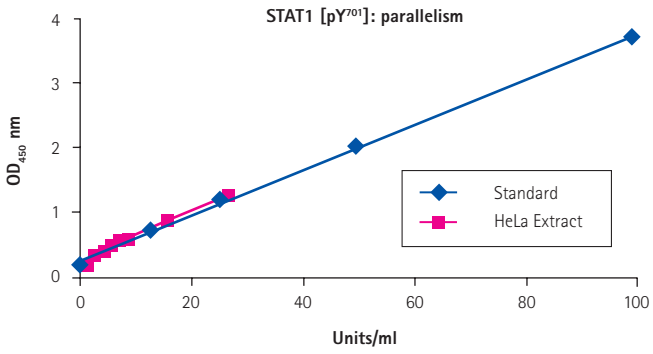
Cat. No. CBA034 **1 kit**

PhosphoDetect™ STAT1 (pTyr^{701}) ELISA Kit

Format: 96-well plate
Sensitivity: <0.9 Unit/ml
Assay range: 1.6-100 units/ml
Assay time: 4 h
Sample type: Cells

A solid phase sandwich ELISA kit suitable for the detection and quantitation of STAT1 phosphorylated at Tyr^{701}. A monoclonal antibody specific for STAT1, regardless of its phosphorylation state, is coated on to plate. A rabbit antibody specific for STAT1 phosphorylated at Tyr^{701} is used as the detection antibody. This kit is designed for use with human cells and tissues.

Cat. No. CBA035 **1 kit**



Natural STAT1 (pTyr^{701}) from IFN-γ-treated HeLa cell lysate was serially diluted in standard diluent buffer. The O.D. of each dilution was plotted against STAT1 (pTyr^{701}) standard curve.

JAK/STAT Pathway products

Inhibitors

Product	Cat. No.	Comments	Size	Price
AG490	658401	A potent inhibitor of EGFR tyrosine kinase autophosphorylation (IC_{50} = 100 nM) and JAK family. Selectively inhibits JAK2 and the autokinase activity of JAK3. *Purity:≥98% by HPLC.* M.W. 294.3	5 mg	
AG490	658408	A cell-permeable, *m*-trifluoromethyl derivative of AG 490 (Cat. No. 658401) that inhibits IL-7-induced JAK3 tyrosine phosphorylation in 2E8 cells. *Purity:≥98% by HPLC.* M.W. 362.3	10 mg	
Cucurbitacin I, *Cucumis sativus L.*	238590	A cell-permeable, potent, and highly selective inhibitor of Janus kinase/signal transducer and activator of transcription 3 (JAK/STAT3) signaling pathway. Suppresses STAT3 tyrosine phosphorylation in v-Src-transformed NIH 3T3 cells and human lung adenocarcinoma A549 cells (IC_{50} = 500 nM). *Purity:≥95% by HPLC.* M.W. 514.7	1 mg	
JAK Inhibitor I	420099	A potent inhibitor of Janus Protein tyrosine Kinases (JAKs). Displays potent inhibitory activity against JAK1 (IC_{50} = 15 nM for murine JAK1), JAK2 (IC_{50} = 1 nM), JAK3 (K_i = 5 nM), and Tyk2 (IC_{50} = 1 nM). *Purity:≥98% by HPLC.* M.W. 309.3	500 µg	
InSolution™ JAK Inhibitor I	420097	A 10 mM solution of JAK Inhibitor I (Cat. No. 420099) in DMSO. *Purity:≥98% by HPLC.* M.W. 309.3	500 µg	
JAK2 Inhibitor II	420132	A cell-permeable, specific and direct inhibitor of JAK2 autophosphorylation (maximal inhibition at 50 µM in BSC-40 cells overexpressing JAK2). *Purity:≥ 99% by titration.* M.W. 557.5	25 mg	
JAK3 Inhibitor I *	420101	A specific inhibitor of JAK3 (IC_{50} = 78 µM). Does not affect the activity of JAK1, JAK2, ZAP/Syk, or Src tyrosine kinases. *Purity:≥97% by HPLC.* M.W. 297.3	5 mg	
JAK3 Inhibitor II *	420104	A potent, cell-permeable inhibitor of JAK3 that is reported to kill glioblastoma cells (IC_{50} = 813 nM). *Purity:≥97% by HPLC.* M.W. 376.2	5 mg	
JAK3 Inhibitor III *	420106	A potent and specific inhibitor of JAK3 (IC_{50} = 11 µM). *Purity:≥92% by HPLC.* M.W. 455.1	1 mg	
JAK3 Inhibitor IV **	420121	A potent and selective ATP-competitive inhibitor of JAK3 (pIC_{50} of 7.1). Weakly inhibits other tyrosine kinases (pIC_{50} = 5.6 for EGF-R; 4.4 for JAK1). *Purity:≥99% by HPLC.* M.W. 367.9	10 mg	
JAK3 Inhibitor V **	420122	A breakdown product of JAK3 Inhibitor-IV (Cat. No. 420121) with similar inhibitory activities (pIC_{50} = 6.8 for JAK3; 5.0 for EGF-R; 4.7 for JAK1). Also inhibits STAT-5 phosphorylation and T-cell proliferation. *Purity:≥98% by HPLC.* M.W. 182.2	10 mg	
JAK3 Inhibitor VI	420126	A cell-permeable, potent inhibitor of JAK3 (IC_{50} = 27 nM) and displays ~16-fold greater selectivity over JAK2. Binds to the enzyme active site and prevents IL-2-induced cellular phosphorylation of JAK3 and STAT5. *Purity:≥98% by HPLC.* M.W. 383.4	5 mg	
JAK3 Inhibitor, Negative Control	420112	A useful negative control compound for JAK3 inhibitors. *Purity:≥92% by HPLC.* M.W. 317.8	500 µg 1 mg	
STAT3 Inhibitor Peptide	573095	A STAT3-SH2 domain binding phosphopeptide that acts as a selective inhibitor of STAT3 signaling with a DB_{50} of 235 µM. Significantly lowers the DNA-binding activity of Stat3 by forming an inactive Stat3:peptide complex and reduces the levels of active STAT3 dimers that can bind DNA. Displays greater affinity for STAT3. *Purity:≥95% by HPLC.* M.W. 870.9	1 mg	
STAT3 Inhibitor Peptide, Cell-Permeable	573096	A cell-permeable analog of the STAT3-SH2 domain-binding phosphopeptide (Cat. No. 573095) that contains a C-terminal membrane translocating sequence. Acts as a highly selective, potent blocker of STAT3 activation. *Purity:≥95% by HPLC.* M.W. 1958.4	1 mg 5 mg	
STAT3 Inhibitor Peptide II, ErbB2-Selective, Cell-Permeable	573092	The SH2 domain-binding motif- (Cat. No. 573095) derived STAT3 inhibiting sequence, PpYL (STAT3BP), is conjugated with a cell-permeant carrier sequence P3-AHNP (Cat. No. 573094), to allow its preferential delivery to ErbB2 high-expressing cells for STAT3 inhibition. *Purity:≥97% by HPLC.* M.W. 3168.5	2 mg	
Tyrene CR4	655230	A cell-permeable, selective inhibitor of JAK2 and Bcr-Abl (IC_{50} ~100-600 nM and 500-700 nM, respectively). *Purity:≥95% by HPLC.* M.W. 320.3	5 mg	
STAT3 Inhibitor V, Stattic	573099	A cell-permeable vinyl-sulfone compound that binds to STAT3-SH2 domain (IC_{50} = 5.1 µM) and blocks STAT3 phosphorylation at Tyr^{705}. Acts as an irreversible inhibitor of STAT3 activation, dimerization and nuclear translocation. *Purity:≥95% by HPLC.* M.W. 211.2	25 mg	

* Sold under license of U.S. Patent 6,080,748 and corresponding patents.
** Sold under license of PCT Application wo 98/22, 103.

Tumor Necrosis Factor-α and Obesity

A number of studies have established a relationship between obesity, insulin resistance, and dyslipidemia. It has been shown that TNF-α is a mediator of insulin resistance in obesity and is over-expressed in adipose tissue of obese rodents and humans. Rodents with genetic obesity and insulin resistance express about 5- to10-fold more TNF-α mRNA, and twice as much TNF-α in their adipose tissue. Elevated levels of TNF-α are shown to down-regulate tyrosine kinase activity of the insulin receptor and diminish the expression of GLUT-4 glucose transporters in obese subjects.

TNF-α elicits its cellular responses via two receptors, TNFR1 (p55) and TNFR2 (p75), which are expressed in relatively different amounts in all mammalian cells. Activation of p55 results in impaired insulin-mediated glucose uptake. However, production of p75, but not p55, is shown to be higher in adipose tissue from human obese subjects. Hence, both receptors appear to be essential for normal glucose homeostasis. Obese (*ob/ob*) mice deficient in both p55 and p75 receptors exhibit an improvement in fasting plasma glucose levels and a reduction in circulating insulin levels when compared to *ob/ob* mice expressing these receptors. Diet induced weight loss reduces the expression of TNF-α and improves insulin sensitivity of tissues.

Antibodies

Product	Cat. No.	Comments	Size	Price
Anti-Tumor Necrosis Factor-α (Ab-1) Mouse mAb (1825.121)	GF31	Monoclonal IgG_1, purified. Immunogen: recombinant human TNF-α. Recognizes the human TNF-α protein. **ELISA, IB, NT**	100 µg	
Anti-Tumor Necrosis Factor-α Rabbit pAb	654250	Polyclonal IgG, purified. Immunogen: recombinant human TNF-α. Recognizes recombinant and monocyte-derived TNF-α. Exhibits some cross-reactivity with lymphotoxin (TNF-β) and mouse TNF-α. **ELISA, FS, IB, NT, PS, RIA**	1 mg	
Anti-Tumor Necrosis Factor-α Rabbit pAb	654300	Polyclonal IgG, purified. Immunogen: recombinant mouse TNF-α. Recognizes recombinant and monocyte-derived TNF-α. Reacts with mouse and rat. **ELISA, IB, NT**	1 ml	
Anti-Tumor Necrosis Factor Receptor (Ab-1) Mouse mAb (16803.1)	GR28L	Monoclonal IgG_1, purified. Immunogen: recombinant human sTNF-R protein. Recognizes the ~55 kDa TNFR in MCF-7 cells. **ELISA, IB, NT**	100 µg	
Anti-Tumor Necrosis Factor Receptor-1 (29-44) Rabbit pAb	654216	Polyclonal IgG. Immunogen: a synthetic peptide corresponding to amino acids 29-44 of human TNFR-1, conjugated to KLH. Recognizes the ~55 kDa TNFR-1 protein. Reacts with canine, human, monkey, rabbit, rat. **ELISA, IB**	100 µg	

ELISA: enzyme-linked immunosorbent assay; **IB**: immunoblotting; **FS**: frozen sections; **mAb**: monoclonal; **NT**: neutralization; **pAb**: polyclonal; **PS**: paraffin sections; **RIA**: radioimmunoassay

Proteins

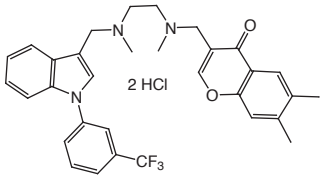
Product	Cat. No.	Comments	Size	Price
Tumor Necrosis Factor-α, Human, Recombinant, *E. coli*	654205	Carrier-free TNF-α. Activity is not species-specific. *Biological activity: ED_{50} = 20-50 pg/ml.* M.W. 17,500	10 µg	
Tumor Necrosis Factor-α, Mouse, Recombinant, *E. coli*	654245	Lyophilized from sterile-filtered PBS, 50 µg BSA/µg TNF-α. *Biological activity: ED_{50} = 20-50 pg/ml.* M.W. 17,000	10 µg	
Tumor Necrosis Factor Receptor I, Soluble, Human, Recombinant, *E. coli*	PF055	sTNFRI neutralizes the biological activity of TNF-α. *Biological Activity: EC_{50} of 0.045-0.09 µg/ml. Purity: >97% by SDS-PAGE.*	25 µg	

Tumor Necrosis Factor-α and Obesity

TNF-α Inhibitors/Antagonists

TNF-α Inhibitor

A cell-permeable indolyl-chromenone compound that rapidly inactivates TNF-α by non-covalently binding to the TNF-α trimer and promoting subunit dissociation and preventing TNF-α binding to its receptor (IC_{50} = 22 µM). Shown to selectively inhibit TNF-α- induced degradation of IkB-α in HeLa cells (IC_{50} = 4.6 µM). *Purity:* ≥ *98% by HPLC*. M.W. 629.6



Cat. No. 654256 **5 mg**

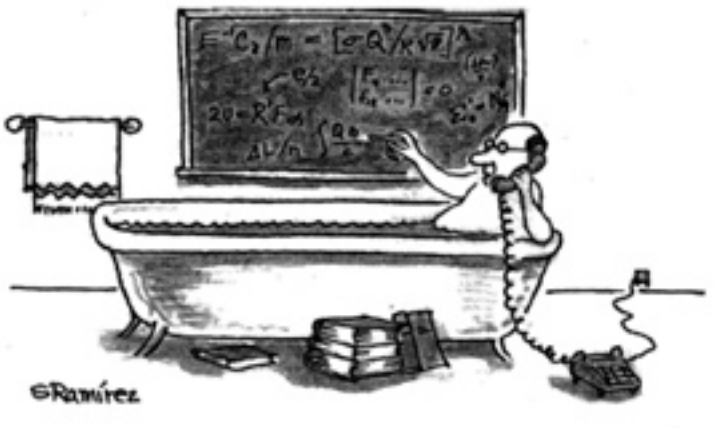
Ref.: He, M.M., et al. 2005. *Science* **310,** 1022.

Tumor Necrosis Factor-α Antagonist

An exocyclic peptidomimetic that acts as a TNF-α antagonist (IC_{50} = 5 µM) in the binding assay. Blocks TNF-α-mediated apoptosis in mouse L929 cells. *Purity:* ≥*95% by HPLC*. M.W.1226.4

Cat. No. 654255 **1 mg**

Ref.: Takasaki, W., et al. 1997. *Nat. Biotechnol.* **15,** 1266.



"With the attention I've been giving to this problem I can almost guarantee a eureka within 48 hours."

Inhibitors of Mitochondrial Function

Product	Cat. No.	Comments	Size	Price
Atractyloside, Dipotassium Salt, *Atractylis gummifera*	189300	Toxic compound originally isolated from the Mediterranean thistle *Atractylis gummifera*. Acts as an ADP/ATP translocase (AAT) inhibitor. Also causes the release of cytochrome *c* from mitochondria. *Purity:≥95% by TLC.* M.W. 803.0	50 mg	
Bongkrekic Acid, Triammonium Salt	203671	Acts as a ligand of the adenine nucleotide translocator. A potent inhibitor of mitochondrial megachannel (permeability transition pore). Prevents the apoptotic breakdown of the inner mitochondrial transmembrane potential ($\Delta\psi_m$), as well as a number of other phenomena linked to apoptosis. *Purity:≥95% by HPLC.* M.W. 537.7	500 µg	
Carbonyl Cyanide *m*-Chlorophenylhydrazone	215911	Protonophore. Uncoupling agent for oxidative phosphorylation that inhibits mitochondrial function. Approximately 100 times more effective than 2,4-dinitrophenol. Binds with cytochrome c oxidase with high affinity (K_d = 270 nM). Inhibits transport processes and depresses growth. *Purity:≥95% by GC.* M.W. 204.6	250 mg	
Carboxyatractyloside, *Atractylis gummifera*	216200	Toxic compound originally isolated from the Mediterranean thistle *Atractylis gummifera*. A highly selective inhibitor of the cytosolic side-specific mitochondrial ADP/ATP carrier (AAC; K_i < 10 nM). *Purity:≥95% by TLC.* M.W. 770.8	5 mg	
CGP-37157	220005	A cell-permeable benzothiazepine derivative of clonazepam that acts as a specific and potent inhibitor of the mitochondrial Na^+/ Ca^{2+} exchanger (IC_{50} = 360 nM). Enhances the export of Ca^{2+} from isolated mitochondria. Also reported to directly inhibit voltagegated Ca^{2+} channels. *Purity:≥98% by TLC.* M.W. 324.2	5 mg	
(-)-Deguelin, *Mundulea sericea*	252740	A cell-permeable rotenoid compound that potently inhibits mitochondrial bioenergetics (IC_{50}=6.9 nM for NADH:ubiquinone oxidoreductase activity in bovine heart ETP). Reported to activate AMPK. *Purity:≥98% by TLC.* M.W. 394.4	5 mg	
F16	341246	A cell-permeable, fluorogenic, delocalized lipophilic cationic compound that acts as a mitochondrial toxin and possesses the dual ability to induce apoptosis as well as necrosis in tumor cells. Preferentially accumulates in mitochondria, inhibits oxidative phosphorylation and causes mitochondrial transmembrane depolarization. The incorporation and localization of F16 can be easily monitored by its fluorescence property. *Purity:≥97% by HPLC.* M.W. 362.2	25 mg	
Hexokinase II VDAC Binding Domain Peptide, Cell-Permeable	376816	A cell-permeable peptide analog of Hexokinase II VDAC binding domain peptide. The internalization domain of the Antennapedia homeoprotein is fused to the methionine amino terminal. Shown to completely detach and translocate HXK2 from mitochondria to the cytosol in HeLa cells at 100 mM. Does not induce Bax translocation or cytochrome c release when used alone. However, it markedly sensitizes cells to cytochrome c release and to the induction of apoptosis when used in combination with a Bax-dependent apoptosis inducer, Indomethacin (Cat. No. 405268). *Purity:≥95% by HPLC.* M.W. 3997.8	1 mg	
Oligomycin	495455	A mixture of A, B, and C isomers. A macrolide antibiotic that inhibits membrane-bound mitochondrial ATPase (F1), preventing phosphoryl group transfer. Induces apoptosis in cultured human lymphoblastoid and other mammalian cells. *Purity:≥90% by HPLC (Mixture of A,B, C isomer).*	10 mg	
Rotenone	557368	A mitochondrial toxin and a potent, reversible, and competitive inhibitor of complex I (NADH-CoQ reductase) of the respiratory chain. Also inhibits cellular proliferation in mouse liver. *Purity:≥98% by TLC.* M.W. 394.4	1 g	
Ru360	557440	A cell-permeable oxygen-bridged dinuclear ruthenium amine complex that has been shown to bind to mitochondria with high affinity (K_d = 340 pM). Specifically blocks Ca^{2+} uptake into mitochondria *in vitro* (IC_{50} = 184 pM) and *in situ* in intact myocytes (complete block after incubation with ~10 mM of Ru360 for 30 min). Does not affect other cellular Ca^{2+} transport processes involved in cardiac muscle contraction, even at micromolar levels. (1 set = 10 × 10 µg). *Purity:≥97% by capillary electrophoresis.* M.W. 550.8	500 µg 1 mg 1 set	
SFK1	565833	A cell-permeable amidine compound that has been shown to interact with Por1p (YVDAC1), a channel protein in the outer mitochondrial membrane, and to modulate ionic balance in *Saccharomyces cerevisiae*. Causes mitochondrially-induced death by stimulating the release of reactive oxygen species (ROS). *Purity:≥95% by HPLC.* M.W. 409.0	10 mg	
Valinomycin, *Streptomyces fulvissimus*	676377	Potassium ionophore of the mobile ion-carrier type that transports alkali metal ions across artificial or biological lipid membranes. Induces K^+ conductivity in cell membranes at concentrations as low as 10^{-8} M. Uncouples oxidative phosphorylation by binding to sites on membranes rich in sulfhydryl groups. Induces apoptosis in murine thymocytes. Also reported to inhibit NGF-induced neuronal differentiation. *Purity:≥93% by HPLC.* M.W. 1111.3	25 mg 100 mg	

Sirtuins and Related Products

Product	Cat. No.	Comments	Size	Price
Sirtinol	566320	A cell-permeable, specific, and a direct inhibitor of the sirtuin class of histone deacetylase (HDAC) activity. Does not affect human HDAC1. Reported to block Sir2p transcriptional silencing activity *in vivo* (IC_{50} = 25 µM) and NAD-dependent HDAC activity in purified recombinant yeast Sir2p and human SIRT2 *in vitro* (IC_{50} = 68 µM and 38 µM, respectively). *Purity:≥97% by HPLC.* M.W. 394.5	5 mg	
InSolution™ Sirtinol	566321	A 10 mM (1 mg/254 µl) solution of Sirtinol (Cat. No. 566320) in DMSO. *Purity:≥97% by HPLC.* M.W. 394.5	1 mg	
SIRT1/2 Inhibitor IV, Cambinol	566323	A cell-permeable β-naphthol compound that acts as a protein substrate competitive, and NAD-uncompetitive inhibitor of hSIRT1 and hSIRT2 (IC_{50} = 56 µM and 59 µM, respectively) with selectivity over SIRT5 (IC_{42} = 300 µM) and SIRT3,-4,-6 & -7, and class I and class II HDACs. Shown to enhance hyperacetylation of BCL6 and p53, and induce growth arrest and apoptosis. Further, chemosensitizes several cancer cells and displays antitumor activity in mouse xenograft models. *Purity:≥95% by HPLC.* M.W. 360.4	5 mg	
Resveratrol	554325	A phenolic product with antifungal, antitumor, and antioxidative properties. Reported to act as a sirtuin activator. *Purity:≥98% by TLC.* M.W. 228.2	25 mg	
Pterostilbene, *Pterocarpus marsupium*	523310	A cell-permeable methoxylated analog of Resveratrol (Cat. No. 554325) that inhibits COX-1 and -2 activities (IC_{50} = 19.8 µM and 83.9 µM respectively). *Purity:≥95% by HPLC.* M.W. 256.3	10 mg	

Leptin, Antibodies for Leptin, and Leptin Receptor

Product	Cat. No.	Comments	Size	Price
Leptin, Human, Recombinant, *E. coli*	429700	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.	1 mg 5 mg	
Leptin, Mouse, Recombinant, *E. coli*	429705	A product of the obese (*ob*) gene that serves as a ligand for the OB receptor (OB-R). Mice with mutations in the *ob* gene have been found to be obese and diabetic and to have reduced activity, metabolism and body temperature. Suppresses insulin secretion by inhibiting activities of Ca^{2+}-dependent PKC isoforms. Reported to reduce hepatic glucose production by blocking phosphoenolpyruvate synthesis.	1 mg 5 mg	
Anti-Leptin Rabbit pAb	431003	Polyclonal IgG, purified. Immunogen: full-length recombinant mouse leptin. Recognizes the ~16 kDa leptin protein. Reacts with mouse, and rat. **ELISA, IB, RIA**	100 µl	
Anti-Leptin Receptor Rabbit pAb	554101	Polyclonal IgG, purified. Immunogen: a synthetic peptide [(C)GSWDIREEK] corresponding to amino acids 83-91 of mouse resistin. Recognizes the resistin protein. Reacts with mouse. **ELISA, IB**	100 µl	
Anti-Leptin Receptor Rabbit pAb	431005	Polyclonal IgG, purified. Immunogen: a synthetic peptide corresponding to a 15-amino acid sequence near the N-terminus of murine leptin receptor. Recognizes the ~150 kDa leptin receptor protein. Does not cross-react with gp130. Reacts with mouse and rat **ELISA, IB**	50 µg	
PhosphoDetect™ Anti-Leptin Receptor ($pTyr^{985}$) Rabbit pAb	431006	Polyclonal IgG, purified. Immunogen: a synthetic phosphopeptide [(C)QPSVKpYATLVS] corresponding to amino acids 980-990 surrounding the Tyr^{985} phosphorylation site of mouse leptin receptor, conjugated to KLH. Recognizes the ~150 kDa leptin receptor protein phosphorylated at Tyr^{985}. Reacts with human and mouse. **IB, IP**	50 µg	

ELISA: enzyme-linked immunosorbent assay; **IB**: immunoblotting; **IP**: immunoprecipitation; **RIA**: radioimmunoassay; **pAb**: polyclonal

Antibodies to Orexins

Product	Cat. No.	Comments	Size	Price
Anti-Orexin A (14-33) (Ab-1) Rabbit pAb	PC345	Polyclonal IgG, purified. Immunogen: a synthetic peptide 33 corresponding to amino acids 14-33 of human orexin A. Recognizes orexin A in mouse and rat brain. Supplied with a control peptide. Reacts with bovine, human, mouse, and rat. **ELISA, FS, IF**	100 µg	
Anti-Orexin A (14-33) (Ab-2) Rabbit pAb	PC362	Polyclonal IgG, undiluted serum. Immunogen: a synthetic peptide corresponding to amino acids 14-33 of human orexin A. Recognizes orexin A in mouse and rat brain. Supplied with a control peptide. Reacts with bovine, human, mouse, and rat. **ELISA, FFS, FS, IF**	100 µl	
Anti-Orexin B (6-24) (Ab-1) Rabbit pAb	PC346	Polyclonal IgG, purified. Immunogen: a synthetic peptide corresponding to amino acids 6-24 of human orexin B, conjugated to KLH. Recognizes orexin B in mouse and rat brain. Supplied with a control peptide. Reacts with human, mouse, and rat. **FS, IF**	25 µg	

ELISA: enzyme-linked immunosorbent assay; **FFS**: free-floating sections; **FS**: frozen sections; **IF**: immunofluorescence; **pAb**: polyclonal

Resistin and Antibodies to Resistin

Product	Cat. No.	Comments	Size	Price
Resistin, Human, Recombinant, *E. coli*	PF138	Recombinant, human resistin expressed in and purified from *E. coli*. A dimeric protein secreted by adipocytes. Resistin may be an important link between obesity and type II diabetes; levels of resistin have been shown to be altered in animal models of diabetes. Contains ≤0.1 ng endotoxin per µg resistin. *Purity:≥98% by SDS-PAGE.* M.W. 19,500	25 µg	
Resistin, Murine, Recombinant, *E. coli*	PF139	A dimeric protein secreted by adipocytes. Resistin may be an important link between obesity and type II diabetes; levels of resistin have been shown to be altered in animal models of diabetes. Contains ≤0.1 ng endotoxin per µg resistin. *Purity:≥98% by SDS-PAGE.* M.W. 20,200	25 µg	
Anti-Resistin (83-91) Rabbit pAb	554101	Polyclonal IgG, purified. Immunogen used was a synthetic peptide corresponding to amino acids 83-91 of mouse resistin. Recognizes mouse resistin. **ELISA, IB**	100 µl	

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

Peptides for Diabetes and Obesity Research

Product	Cat. No.	Comments	Size	Price
Galanin, Porcine	05-23-2350	A biologically active neuropeptide that has been shown to inhibit secretion of somatostatin, insulin, and pancreatic polypeptide. Also induces repolarization and reduces free Ca^{2+} due to interference with voltage-activated Ca^{2+} channels. *Purity:≥97% by HPLC.* M.W. 3210.6	0.5 mg 1 mg	
Neuropeptide Y (Porcine)	05-22-2000	An inhibitor of Ca^{2+}-activated K^+ channels in vascular smooth muscle cells. Stimulates Na^+,K^+-ATPase activity in renal tubules. Strong inhibitor of both cholecystokinin- and secretin-stimulated pancreatic secretion.	0.1 mg 0.5 mg	
Neuropeptide Y, Human	05-23-2005	A potent vasoconstrictor. Reversibly inhibits Ca^{2+}-activated K^+ channels in vascular smooth muscle cells. *Purity:≥97% by HPLC.* M.W. 4271.7	0.5 mg 1 mg	
Obestatin, Human, Synthetic	494125	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	2 mg	
PACAP 27 Amide, Ovine	05-23-2151	Increases cAMP levels in a dose-dependent manner (EC_{50} = 4.7 nM). Increases tyrosine hydroxylase expression in chromaffin cells. *Purity:≥98% by HPLC.* M.W. 3147.7	0.5 mg	
PACAP 38, Ovine	05-23-2150	More active than vasoactive intestinal peptide (VIP) in stimulating adenylate cyclase (EC_{50} = 7 nM). *Purity:≥96% by HPLC.* M.W. 4534.3	0.1 mg 1 mg	
Somatostatin	05-23-0850	Cyclic tetradecapeptide. Inhibits the release of growth hormone, insulin, and glucagon. Inhibits voltage-gated Ca^{2+} channels.	1 mg 5 mg	

C-Reactive Proteins

Product	Cat. No.	Comments	Size	Price
Anti-C-Reactive Protein Rabbit pAb	235752	Polyclonal IgG, purified. Immunogen: purified human CRP. Recognizes C-reactive protein. Does not exhibit cross-reactivity against normal human serum. Reacts with human. Suitable for ELISA, immunoprecipitation, and radioimmunoassay.	1 ml	
C-Reactive Protein, Human Ascites	236600	A major acute-phase plasma protein that is dramatically elevated in patients with acute-phase conditions. Composed of five identical noncovalently linked subunits. Exhibits Ca^{2+}-dependent binding to a variety of substrates. Suitable for immunological studies. In purified states and in plasma the monomeric form (M.W. ~21 kDa) aggregates as a cyclic pentamer. *Purity: single band by SDS-PAGE.* M.W. 23,000	1 mg	
C-Reactive Protein, Human Serum, High Purity	236603	A major acute-phase plasma protein that is dramatically elevated in patients with acute-phase conditions. Composed of five identical noncovalently linked subunits. Exhibits Ca^{2+}-dependent binding to a variety of substrates. Suitable for immunological studies. In purified states and in plasma the monomeric form (M.W. ~21 kDa) aggregates as a cyclic pentamer. Intended for use as a calibration standard for assays of CRP, for structural and functional studies, and as an antigen for production of antisera. Calibrated by electroimmunoassay against WHO reference standard or equivalent. *Purity: ≥99% by SDS-PAGE.* M.W. 23,000	100 µg	
C-Reactive Protein, Human, Recombinant, *E. coli*	236608	A major acute-phase plasma protein that is dramatically elevated in patients with acute-phase conditions. Composed of five identical noncovalently linked subunits. Exhibits Ca^{2+}-dependent binding to a variety of substrates. Important in diagnosis of rheumatoid arthritis. Suitable for immunological studies. In purified states and in plasma the monomeric form (M.W. ~21 kDa) aggregates as a cyclic pentamer. *Purity: single band by SDS-PAGE.* M.W. 23,000	1 mg	

Other Products of Interest in Diabetes and Obesity

Product	Cat. No.	Comments	Size	Price
Anti-Acrp30 (18-32; 187-200) Rabbit pAb (Anti-adipoectin)	107920	Polyclonal IgG, purified. Immunogen: two synthetic peptides (EDDVTTTEELAPALV;FTYDQYQ EKNVDQA) corresponding to amino acids 18-32 and 187-200 of mouse Acrp30. Recognizes the ~30 kDa Acrp protein in mouse serum. Reacts with mouse. **IB, IP**	200 µg	
Anti-Agouti-Related Protein Rabbit pAb	122402	Polyclonal IgG, purified. Immunogen: a synthetic peptide corresponding to a 15-amino acid sequence at the C-terminus of mouse AGRP. Recognizes the ~13 kDa AGRP. Does not cross-react with Agouti, TUbby, TULP-1, or TULP-2. Reacts with mouse. **ELISA, IB, IF, IH**	50 µg	
Anti-Cholecystokinin-8 (26-33) Rabbit pAb	PC206L	Polyclonal IgG, undiluted serum. Immunogen: a synthetic peptide corresponding to amino acids 26-33 of sulfated rat cholecystokinin-8. Recognizes the cholecystokinin-8 protein. Reacts with rat. **FS, IF**	100 µl	
L-(–)-Epinephrine-(+)-bitartrate	324900	α, β-Adrenergic receptor agonist. Has positive chronotropic and inotropic effects on heart muscle. Activates adenylate cyclase to generate cAMP from ATP. *Purity:≥95% by TLC.* M.W. 333.3	100 mg	
L-(–)-Norepinephrine-(+)-bitartrate	489350	α, β-Adrenergic agonist. A vasoconstrictive agent that causes down-regulation of angiotensin II receptors. Oxidation sensitive. *Purity:≥99% by titration.* M.W. 319.3	100 mg	
Glycogen Phosphorylase Inhibitor	361515	A cell-permeable urea compound that acts as a potent and AMP-competitive inhibitor of glycogen phosphorylase (GP; IC_{50} = 53 nM). Shown to inhibit glucagon-induced glyocgenolysis both in hepatocytes (IC_{50} = 380 nM) *in vitro* and in rats (5 mg/kg, iv) *in vivo*. *Purity: ≥98% by HPLC.* M.W. 412.8	1 mg	
Growth Hormone, Human Pituitary, Iodination Grade	869008	A single chain polypeptide hormone that is essential for growth. Increases fat mobilization. *Activity: ≥5 IU/mg.* M.W. 21,700	50 µg 100 µg	
Z-Guggulsterone	370690	A synthetic form of the guggul tree plant steroid that exhibits an ability to lower LDL cholesterol and triglyceride levels. Acts as a selective antagonist of farnesoid X receptor (FXR) and inhibits FXR transactivation (IC_{50} = 10 µM in the presence of 100 µM chenodeoxycholic acid). Does not activate or inhibit transactivation of liver X receptor α (LXRα), peroxisome proliferator activated receptor γ (PPARγ), or retinoid X receptor α (RXRα). *Purity: single spot by TLC.* M.W. 312.5	10 mg 25 mg	
MIF Antagonist, ISO-1	475837	A cell-permeable anti-inflammatory, anti-diabetogenic agent that inhibits MIF tautomerase activity by binding to its catalytic active site (IC_{50} = 7 µM for D-dopachrome tautomerase) and suppresses the production of TNFα, PGE_2 and COX-2 in human monocytes, and arachidonic acid in RAW 264.7 macrophages. *Purity: ≥95% by HPLC.* M.W. 235.1	5 mg	

ELISA: enzyme-linked immunosorbent assay; **FS**: frozen sections; **IB**: immunoblotting; **IF**: immunofluorescence; **IH**: immunohistochemistry; **IP**: immunoprecipitation; **pAb**: polyclonal

Other Products of Interest in Diabetes and Obesity

Product	Cat. No.	Comments	Size	Price
NBI-31772	479830	A non-peptide ligand that exhibits high-affinity (K_i ~ 1 - 17 nM) towards all six human insulin-like growth factor-I binding proteins (IGFBPs). Displaces insulin-like growth factor-I (IGF-I) from the IGF-I:IGFBP complex in 3T3 fibroblasts; however, it does not interact with the IGF receptors. *Purity:≥97% by HPLC.* M.W. 341.3	5 mg	
PKC_{β} Inhibitor	539654	A potent, ATP-competitive inhibitor of PKC_{β} (IC_{50} = 5 nM and 21nM for human $PKC_{\beta II}$ and $_{\beta I}$, respectively). Inhibits insulin-stimulated uptake of 2-deoxyglucose. *Purity:≥90% by HPLC.* M.W. 411.5	500 µg	
$PKC_{\beta II}$/EGFR Inhibitor	539652	A cell-permeable, potent and ATP-competitive inhibitor of EGFR and PKC isozymes α, β_I, and β_{II} (IC_{50} = 0.7 µM, 1.9 µM, 3.8 µM, and 0.41 µM, respectively). Inhibits insulin-stimulated uptake of 2-deoxyglucose. *Purity:≥98% by HPLC.* M.W. 365.3	2 mg	
SecinH3	565725	A cell-permeable inhibitor of Sec7-specific guanine nucleotide exchange factor activity and Drosophila Step (Steppke) protein. Blocks insulin signaling pathway by selectively inhibiting pIRS-1 by IR. *Purity:≥98% by HPLC.* M.W. 460.5	5 mg	
Sphingosine Kinase Inhibitor	567731	A cell-permeable, potent, non-ATP-competitive, and highly specific inhibitor of sphingosine kinase (IC_{50} = 500 nM for GST-hSK). *Purity:≥98% by HPLC.* M.W. 339.2	10 mg	
Thyroid Stimulating Hormone, Bovine Pituitary	609385	Glycoprotein hormone that exerts mild, continuous stimulation on the thyroid, resulting in maintenance of activity. Its secretion is inhibited by Somatostatin (Cat. No. 05-23-0850). *Potency:≥0.7 IU/mg as measured against the WHO standard or equivalent.*	5 IU	
Thyroid Stimulating Hormone, Human Pituitary, Iodination Grade	869006	Glycoprotein hormone that exerts mild, continuous stimulation on the thyroid, resulting in maintenance of activity. Its secretion is inhibited by Somatostatin. *Immunopotency:≥6 IU/mg (WHO 1st IRP 68/38).*	10 µg 50 µg 100 µg	
Thyroxine-Binding Globulin, Human	612075	Liver glycoprotein and a major thyroid hormone carrier in serum. Exhibits high sequence similarity with α_1-antitrypsin. Its affinity for the hormone is thought to be temperature-sensitive. *Purity:≥99% by SDS-PAGE.* M.W. 54,000-64,000	250 µg	
Thyroglobulin, Bovine Thyroid Gland	609310	A glycoprotein consisting of two polypeptide homodimers of 330 kDa each. An excellent source of N-linked glycans of various structures, including sialylated core fucose and oligomannose oligosaccharides. Gal-3-SO_4 and GalNAc-6-SO_4 residues, located in a single multi-branched complex type glycan, have been reported in calf thymus and human proteins. *Purity:≥90% by SDS-PAGE.* M.W. 660,000	100 mg	
Thyroglobulin, Human Thyroid	609312	A homodimeric glycoprotein consisting of two polypeptide monomers of molecular weight 330,000. This protein is an excellent source of N-linked glycans of various structures, including sialylated core fucose and oligomannose oligosaccharides. Also, Gal-3-SO_4 and GalNAc-6-SO_4 residues located in a single multi-branched complex type glycan have been reported in calf thymus and human proteins. *Purity:≥96% by PAGE.* M.W. 660,000	1 mg	

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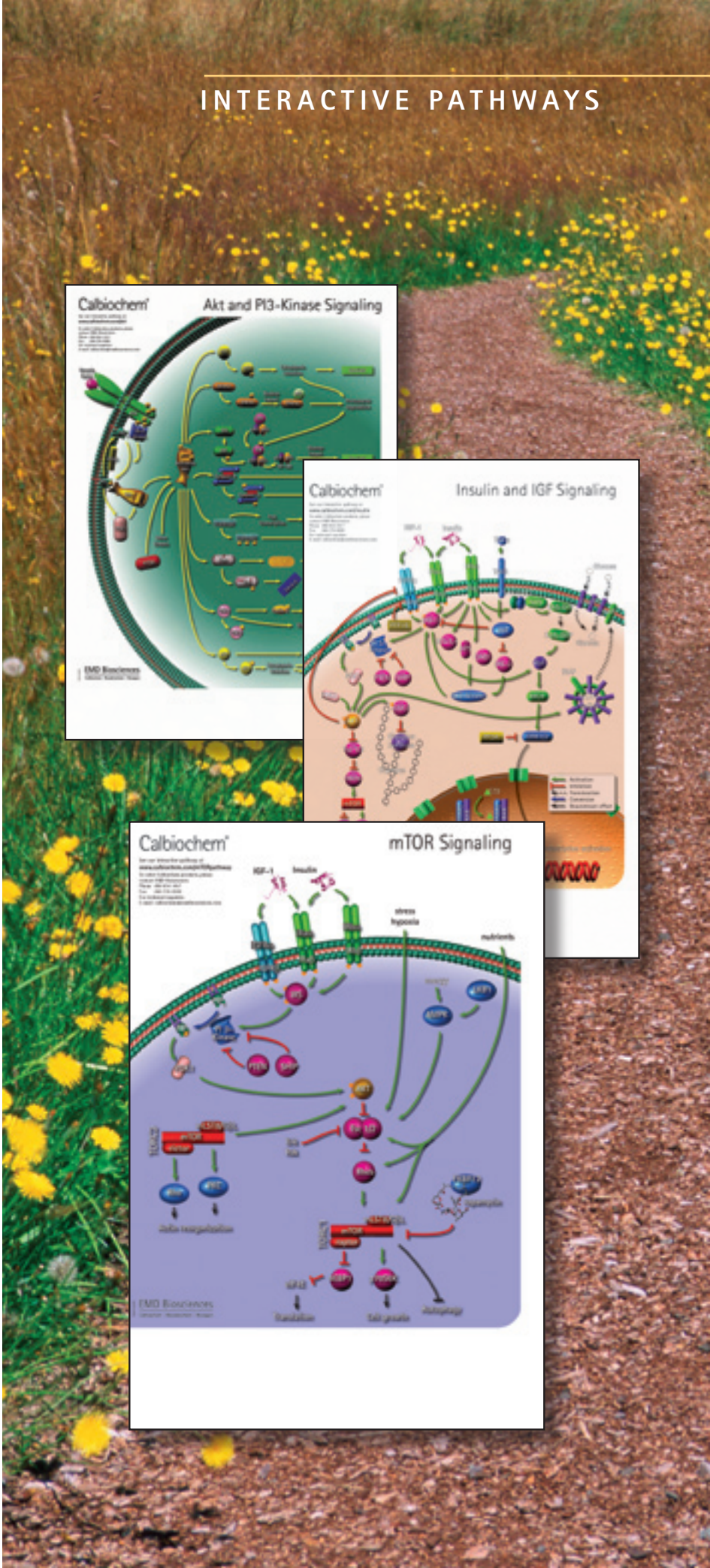

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