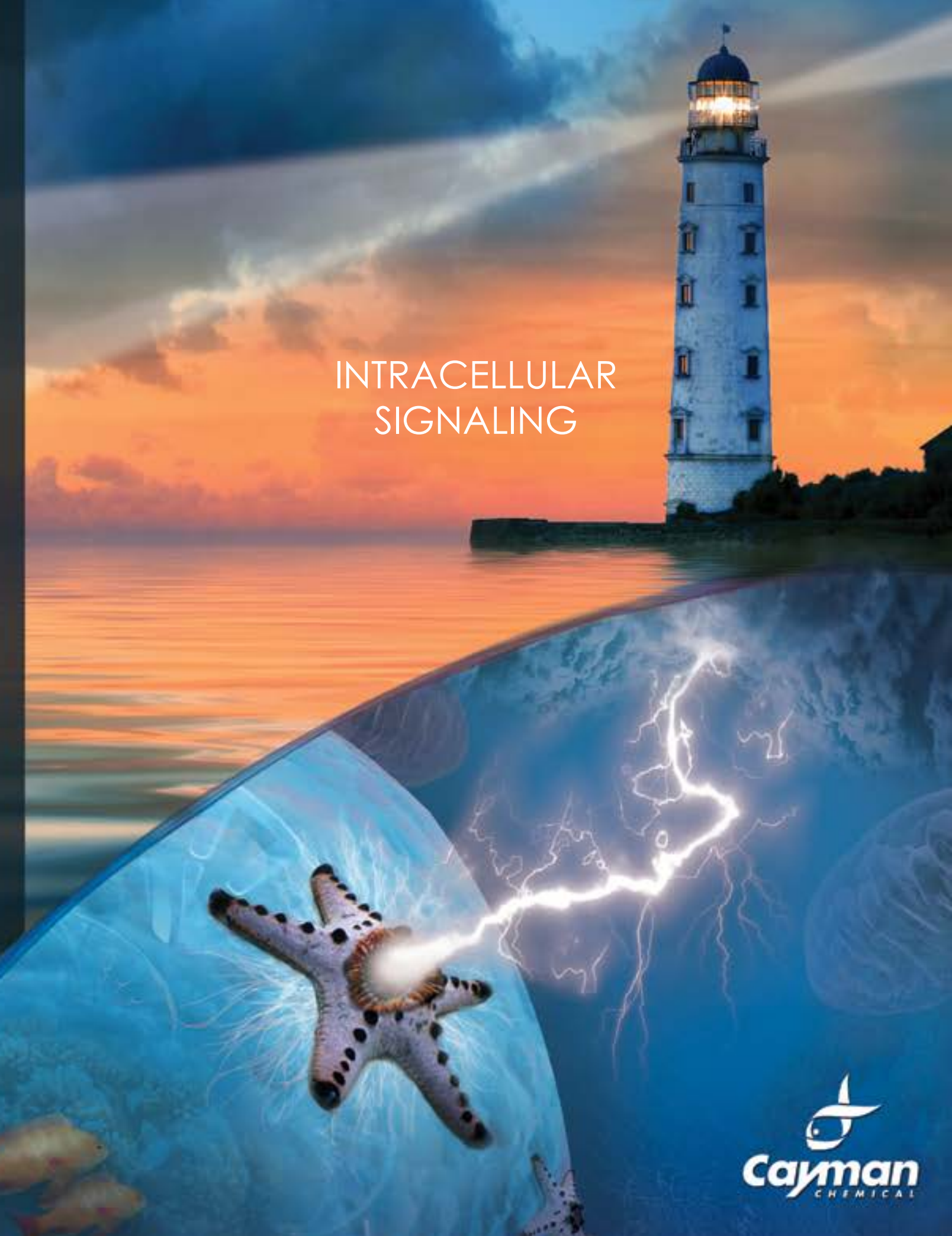
INTRACELLULAR
SIGNALING
Cayman
CHEMICAL

Introduction to
Intracellular Signaling

Artistically, intracellular signals travel at lightning bolt speed from the cell surface to subcellular targets. In reality, these signals are physical and molecular entities. They are the cytoplasmic and intranuclear modulations that maintain stability or initiate change. They are the chemicals and kinases which determine cellular life and death. Each cell must convert perceived hormones, stresses, and environmental cues into effective messages, the instructions that dictate the cell's behavior or response. Ultimately, all diseases can be viewed as errors in signaling: a protein is missing, oxidants aren't neutralized, a kinase stays on too long.

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Intracellular Signaling to Histone Deacetylases

by [Thomas G. Brock, Ph.D.]

Some seventy years ago, toward the end of World War II, food supplies were severely depleted in Europe. During the winter of 1944-1945, a German blockade cut off food shipments into the Netherlands, resulting in the Dutch famine of 1944. From this emerged the Dutch Famine Birth Cohort, consisting of 2,414 individuals who were born immediately before, during, or after the "Hungerwinter" and evaluated at ages 50 and 58 for disease history. Exposure to famine during gestation led to a higher cumulative incidence and earlier onset of coronary artery disease than was found for those not exposed to famine during gestation.[1] This correlative study suggests that famine, in some way, produced epigenetic changes that impacted cardiovascular health many years later. Numerous additional studies of this cohort have been published. However, none can delineate the molecular links between exposure to famine and putative epigenetic changes. This article touches on those links, the intracellular signals that affect epigenetic enzymes.

Post-translational Modification of SIRT1

Curiously, while famine is bad for health, lifespan can be increased through a dietary regimen of caloric restriction without malnutrition.[2] Sirtuins, including Sir2 in yeast and its homolog SIRT1 in mammals, have been proposed to mediate the effect of caloric restriction.[3] A key unanswered question, however, remains: how does caloric restriction alter sirtuin activity? Or, more broadly, what intracellular signaling pathways directly change the function of these enzymes?

Several sirtuins, including those linked to longevity, have NAD^+-dependent protein deacetylase activity, meaning that they remove acetyl groups from proteins, using NAD^+ as the acetyl acceptor. As members of the larger class of proteins known as histone deacetylases (HDACs), sirtuins modify histones, which can alter chromatin compaction and gene expression. They also deacetylate many non-histone proteins: SIRT1 targets p53, HIF-1, Akt1, Myc, FOXO1, Taf1B, Dnmt1, pCAF, Myod1, Suv39H1, Tip60, Rb1, Smad7, Irs2, RelA, and others. SIRT1, then, is an important point of regulation for several intracellular signaling pathways. SIRT1 expression is subject to regulation and SIRT1 activity can be affected by the availability of its co-factor, NAD^+. In addition, SIRT1 has nuclear import and export sequences (Figure 1), which can impact the access of SIRT1 to its targets. However, in what ways can SIRT1 be regulated by post-translational modification (PTM)?

Phosphorylation is a major form of PTM on SIRT1. The MAP kinase JNK1, which can be activated by cellular stresses, phosphorylates SIRT1 on three residues. H_2O_2, which activates JNK1, promotes nuclear accumulation of SIRT1 and increases its deacetylation activity toward histone H3 but, surprisingly, not toward p53. In mice, persistent JNK1 activation and phosphorylation of SIRT1 at S46 is followed by ubiquitination and proteasomal degradation of SIRT1. Casein kinase 2 (CK2) can, like JNK1, be activated by stress. Ionizing radiation induces CK2-mediated phosphorylation of SIRT1 on multiple sites. This phosphorylation of SIRT1 increases deacetylation of p53 and protection from apoptosis after DNA damage.[4] Phosphorylation of SIRT1 by PKA increases the rate of deacetylation of PGC-1α and augments fatty acid oxidation. Phosphorylation of SIRT1 by cyclin B/CDK1 appears to be required for normal cell cycle progression. The dual specificity tyrosine phosphorylation-regulated kinases DYRK1A and DYRK3 target SIRT1, which increases deacetylation of p53 and protects against DNA damage-induced cell death. Phospho-peptide mapping of human SIRT1 reveals that 13 residues are phosphorylated when SIRT1 is overexpressed in embryonic stem cells. Phospho-proteomic information compiled at PhosphoSitePlus indicates that at least 28 residues on human SIRT1 are phosphorylated. Apparently, nuclear proteins, including SIRT1, have high phosphorylation site occupancy during mitosis, which may account for some post-translational modification of this HDAC.

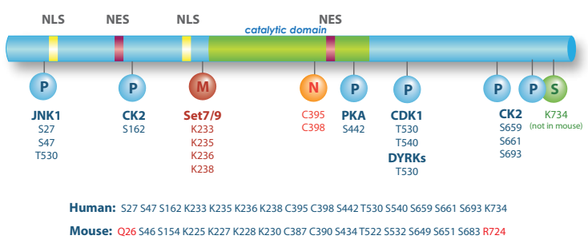

Figure 1. Human SIRT1 has two consensus nuclear localization signals (NLS) and two nuclear export signals (NES), one of which is nested in the catalytic domain. SIRT1 can be phosphorylated (P) by JNK1, CK2, PKA, CDK1, and DYRKs, methylated (M) by Set7/9, nitrosylated (N), and sumoylated (S). Mouse amino acids corresponding to the human residues are given at bottom.

SIRT1 is also modified by methylation, nitrosylation, and sumoylation. SET7/9 methylates four adjacent residues between an NLS and the catalytic domain, but this does not alter activity.[5] Interestingly, nitrosylation of GAPDH, as occurs following induction of iNOS, induces the import of S-nitrosylated GAPDH (SNO-GAPDH) into the nucleus, where it interacts with and transnitrosylates nuclear proteins, including SIRT1.[6] This strongly inhibits SIRT1's deacetylase activity. Finally, human SIRT1 is constitutively sumoylated on K734, with removal of SUMO mediated by SENP1 following either UV radiation or hydrogen peroxide treatment. Mutation of K734 or desumoylation of SIRT1 decreases deacetylase activity. Curiously, mouse SIRT1 has an arginine at the homologous site, so it is not sumoylated.

Modification of Class I HDACs

In humans, HDACs are divided into four classes: class I (HDAC1, 2, 3, 8), class IIa (HDAC 4, 5, 7, 9) and class IIb (HDAC6, 10), class III (SIRT1-3, 5, 6), and class IV (HDAC11). Of the class I HDACs, HDAC1, 2, and 8 are found primarily in the nucleus, whereas HDAC3 can be found in both the nucleus and the cytoplasm. All are distributed ubiquitously, although their roles and regulation may differ between cell types.

HDAC	aa	PTM	sequence	HDAC	aa	PTM	sequence
HDAC1	K218	acet	GAGKGKY	**HDAC2**	S394	phos-CK2	HEDSGDE
	K220	acet	GKGKYVA		S411	phos-CK2	IRASDKR
	S393	phos	PEESGDE		S422	phos-CK2	EEFSDSE
	S421	phos-CK2	EEFSDSE		S424	phos-CK2, JNK	FSDSEDE
	S423	phos-CK2	FSDSEEE		K462	sumo	TDVKEED
	K432	acet	GGRKNSS				
	K438	acet	SNFKKAK				
	K439	acet	NFKKAKR	**HDAC3**	S424	phos-CK2	DKESDVE
	K441	acet	KKAKRVK				
	K444	sumo	KRVKTED				
	K476	sumo	KGVKEEV	**HDAC8**	S39	phos-PKA	KRASMVM

Table 1. The sites of post-translational modification (PTM) on class I HDACs include amino acids (aa) which are acetylated (acet), phosphorylated (phos), or sumoylated (sumo).

Of the four class I HDACs, HDAC1 has been the most intensively studied. Both the human and mouse form contain 482 amino acids and are modified on the same residues, primarily at the C-terminus, away from the catalytic domain (residues 9-321). This HDAC can be acetylated on several lysines (Table 1). Acetylation is mediated by p300, can occur after HDAC1 association with glucocorticoid receptor, and results in heterodimerization of HDAC1 with HDAC2 and a reduction in gene expression. [7] HDAC1 appears to be, at least in part, constitutively sumoylated, which can affect HDAC1 in a variety of ways. Some 295 phospho-proteome analyses of a variety of tissues and cell types have shown that HDAC1 is phosphorylated on S393, suggesting that this site is constitutively phosphorylated. Serines 421 and 423 also are constitutively phosphorylated in cultured Jurkat cells and can be targeted by CK2. Interestingly, serum can activate CK2,[8] suggesting that phosphorylation of these sites may be common in cultured cells. Substitution of these residues with alanine, preventing their phosphorylation, reduces enzymatic activity.

The CK2 sites on HDAC1 are conserved on HDAC2 and can be phosphorylated by CK2 which has been activated by cigarette smoke extract or acrolein (in human bronchial epithelial cells) or by hypertrophic stimuli (in cardiomyocytes).[9] These stimuli also induce CK2-mediated phosphorylation of S394 and S411 on HDAC2. All-*trans* retinoic acid causes JNK-mediated phosphorylation of S424 on HDAC2 in vascular smooth muscle cells, resulting in dissociation of HDAC2 from the transcription factor KLF4 and derepression of transcription. On HDAC3, only a unique C-terminal site is phosphorylated by CK2. Phosphorylation of S39 on HDAC8, positioned within the catalytic domain, is directed by PKA and results in decreased activity toward histones H3 and H4. Finally, sumoylation of K462 on HDAC2 by SUMO1 allows binding and deacetylation of p53 and reduced apoptosis following DNA damage.[10]

Modification of Class II HDACs

Unlike class I HDACs, class II HDACs shuttle in and out of the nucleus and this affords a novel mechanism of regulation. HDAC4, the best-studied of this group, has diverse actions, including the regulation of myocyte differentiation and function by repressing MEF2 transcription factors (Figure 2).[11] Phosphorylation of HDAC4 can provide binding sites for 14-3-3 proteins. These small proteins cap specific phophoserine sites on select proteins, altering the rate of dephosphorylation and impacting protein function. Binding of 14-3-3 to HDAC4 appears to happen within the nucleus, but this interaction prevents nuclear import of the HDAC4/14-3-3 complex, resulting in accumulation in the cytoplasm. As HDAC4 cannot act on histones while in the cytoplasm, HDAC4-repressed genes, like those controlled by MEF2s, become derepressed. Similar patterns occur in all class IIa HDACs (HDAC4, 5, 7, and 9).[12] Phosphatases, including PP1 and PP2A, dephosphorylate these HDACs, releasing 14-3-3 and allowing nuclear import. Caspase-3 cleavage of HDAC4 generates an N-terminal fragment which contains an NLS but lacks HDAC activity. This piece is imported into the nucleus, where it can repress MEF2-mediated gene expression. HDAC4 can be phosphorylated on over twenty residues, as well as acetylated, ubiquitinated, and sumoylated. Phosphorylation can be by CaMK2, MARK2, GSK3β, PKC, Aurora B, EMK, or TAK1. Sumoylation, which occurs on K559 of HDAC4, is mediated by SUMO-1 in the nucleus. Ubiquitinylation of HDAC4, followed by degradation, is elicited by serum starvation and prevented by GSK3β-mediated phosphorylation of S298, a site that is dephosphorylated by PP2A.[13] Thus, HDAC4, representative of class IIa HDACs, cycles between the cytoplasm and nucleus, providing a moving target for an assortment of modifying enzymes.

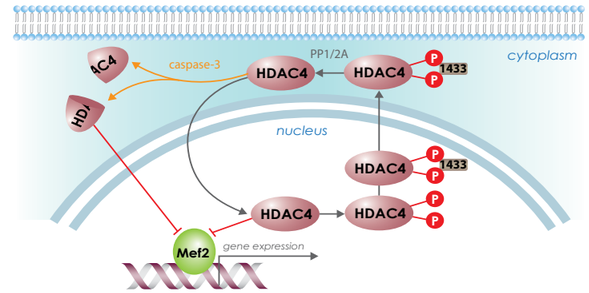

Figure 2. Class IIa HDACs, like HDAC4, repress gene expression when in the nucleus. Phosphorylation, which permits binding by 14-3-3 and inhibits nuclear import, can be reversed by phosphatases. Also, caspase-3 can cleave HDAC4, generating a fragment which can still suppress transcription.

Of the two class IIb HDACs, only HDAC6, a predominantly cytoplasmic protein, has been linked to specific kinases. EGFR-mediated phosphorylation of HDAC6 on Y570 decreases activity, increasing acetylation of α-tubulin. GSK3β appears to phosphorylate HDAC6 and in this way modulate mitochondrial transport, while CK2 targets S458 to increase deacetylase activity, which is needed to form and clear aggresomes.

Clearly, HDACs are dynamically modulated by diverse intracellular signaling pathways, both in the cytoplasm and within the nucleus. Moreover, we are only beginning to understand the importance of this form of HDAC regulation on cell function. It will be interesting to see how this field develops in the next few years. n

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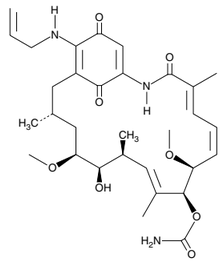
Biochemicals

17-AAG 11039

[75747-14-7] BMS 722782, CP 127,374, KOS 953, NSC 330507, Tanespimycin
MF: $C_{31}H_{43}N_3O_8$ **FW:** 585.7 **Purity:** ≥98%
A solution in methanol **Stability:** ≥2 years at -20°C
Summary: An analog of geldanamycin which has potent *in vivo* activity and reduced toxicity; has diverse anti-tumor actions; promotes the degradation of HER2 and induces growth arrest and apoptosis in breast cancer cells overexpressing HER2 (IC_{50} = 4-72 nM)

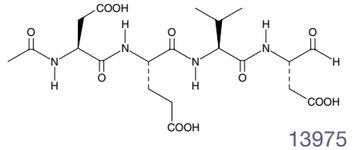
100 µg
1 mg



N-Ac-Asp-Glu-Val-Asp-CHO 10017

[184179-08-6] Ac-DEVD-CHO
MF: $C_{20}H_{30}N_4O_{11}$ **FW:** 502.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent and selective inhibitor of caspase-3

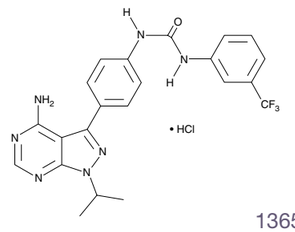
500 µg
1 mg
5 mg
10 mg



AD57 (hydrochloride) 13975

MF: $C_{22}H_{20}F_3N_7O$ • HCl **FW:** 491.9 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A polypharmacological cancer therapeutic; potently inhibits Ret (IC_{50} = 2 nM) and reduces the activity of numerous other kinases by more than 80% when given at 1 µM in *Drosophila*; interferes with kinases downstream of Ret, including Src, Raf, and S6K

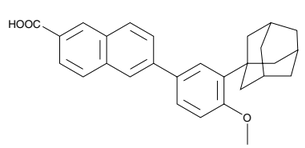
1 mg
5 mg
10 mg



Adapalene 13655

[106685-40-9] CD 271, Differin
MF: $C_{28}H_{28}O_3$ **FW:** 412.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A selective agonist of RAR-β and RAR-γ (K_ds = 34 and 130 nM, respectively) commonly used for the study of the pathogenesis and treatment of acne vulgaris; dose-dependently (0.1-10 µM) inhibits sebocyte growth, proliferation, and differentiation

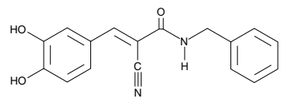
100 mg
250 mg
500 mg
1 g



AG-490 10010311

[133550-30-8]
MF: $C_{17}H_{14}N_2O_3$ **FW:** 294.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An inhibitor of JAK2 activity that selectively blocks leukemic cell growth *in vitro* and *in vivo* by inducing programmed cell death, with no deleterious effect on normal hematopoiesis; almost completely blocks growth of all pre-B acute leukemia cells at a concentration of 5 µM

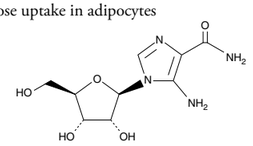
5 mg
10 mg
25 mg
50 mg



AICAR 10010241

[2627-69-2] Acadesine, AICA Riboside, NSC 105823
MF: $C_9H_{14}N_4O_5$ **FW:** 258.2 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A selective activator of AMPK; inhibits synthesis of fatty acids and sterols in hepatocytes and insulin-stimulated glucose uptake in adipocytes

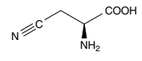
5 mg
10 mg
50 mg
100 mg



β-cyano-L-Alanine 10010947

[6232-19-5] BCA
MF: $C_4H_6N_2O_2$ **FW:** 114.1 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A reversible inhibitor of the H_2S synthesizing enzyme cystathionine γ lyase; blocks H_2S synthesis in rat liver preparations with an IC_{50} value of 6.5 µM

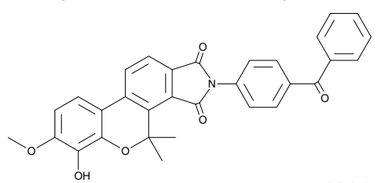
10 mg
50 mg
100 mg
250 mg



Ampkinone 10631

[1233082-79-5]
MF: $C_{31}H_{23}NO_6$ **FW:** 505.5 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A small molecule activator of AMPK that stimulates functional activation of AMPK in cultured muscle cells (EC_{50} = 4.3 µM), enhancing glucose uptake by 3.2-fold; 10 mg/kg up-regulates the activity of AMPK in the liver and muscle of diet-induced obese mice, enhancing insulin sensitivity and increasing the oxidation of adipose tissues

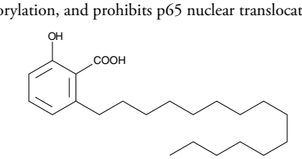
1 mg
5 mg
10 mg



Anacardic Acid 13144

[16611-84-0] 6-pentadecyl Salicylic Acid
MF: $C_{22}H_{36}O_3$ **FW:** 348.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An alkyl salicylic acid isolated from cashew shells; inhibits the HAT activity of p300 and pCAF (IC_{50} = 8.5 and 5 µM, respectively); suppresses NF-κB activation, inhibits IκB-α phosphorylation, and prohibits p65 nuclear translocation

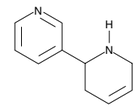
1 mg
5 mg
10 mg



Anatabine 11001

[2743-90-0]
MF: $C_{10}H_{12}N_2$ **FW:** 160.2 **Purity:** ≥95%
A solution in ethanol **Stability:** ≥1 year at -20°C
Summary: A minor alkaloid produced in plants of the Solanaceae family, including tobacco; detection in urine is used as an indicator of tobacco use; diminishes Aβ production, reduces the transcription and protein levels of β-secretase, and dose dependently inhibits NF-κB activation

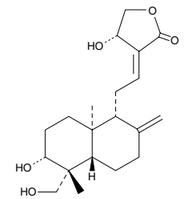
5 mg
10 mg
50 mg
100 mg



Andrographolide 11679

[5508-58-7]
MF: $C_{20}H_{30}O_5$ **FW:** 350.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A diterpenoid compound that inhibits NF-κB binding to DNA promoters and induces expression of the CYP1A enzymes to produce immunosuppressant, antithrombotic, anti-inflammatory, antineoplastic, anti-viral, anti-bacterial, anti-diabetic, anti-oxidative stress, antipyretic, anti-oedematogenic, and anti-nociceptive activities

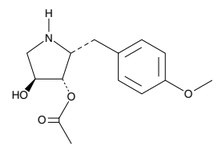
50 mg
100 mg
250 mg
500 mg



Anisomycin 11308

[22862-76-6] Flagecidin, NSC 76712, Wuningmeisu C
MF: $C_{14}H_{19}NO_4$ **FW:** 265.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A pyrrolidine antibiotic produced by *S. griseolus* that inhibits protein and DNA synthesis and activates stress-activated protein kinase, MAPK, and other signal transduction pathways

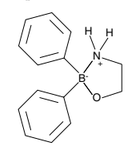
5 mg
10 mg



2-APB 64970

[524-95-8]
MF: $C_{14}H_{16}BNO$ **FW:** 225.1 **Purity:** ≥98%
A crystalline solid **Stability:** ≥1 year at -20°C
Summary: A cell-permeable antagonist of IP_3 receptors

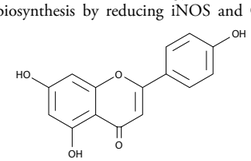
100 mg
1 g



Apigenin 10010275

[520-36-5] Chamomile, Flavone, NSC 83244, Versulin
MF: $C_{15}H_{10}O_5$ **FW:** 270.2 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: Inhibits CK2 activity in the renal cortex with an IC_{50} value of 30 µM; potent inhibitor of NO and PGE_2 biosynthesis by reducing iNOS and COX-2 expression

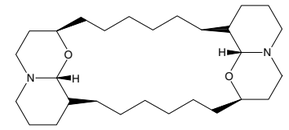
25 mg
50 mg
100 mg
500 mg



Araguspongin B 10006797

[123000-02-2]
MF: $C_{28}H_{51}N_2O_2$ **FW:** 447.4 **Purity:** ≥90%
A clear film **Stability:** ≥1 year at -20°C
Summary: An antagonist of the inositol 1,4,5-trisphosphate receptor (IC_{50} = 0.6 µM)

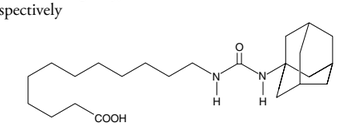
100 µg
250 µg



AUDA 10007927

[479413-70-2]
MF: $C_{23}H_{40}N_2O_3$ **FW:** 392.6 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An inhibitor of sEH exhibiting IC_{50} values of 18 and 69 nM for the mouse and human enzymes, respectively

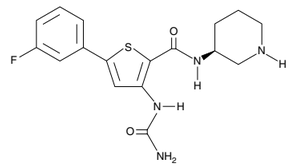
5 mg
10 mg
50 mg
100 mg



AZD 7762 11491

[860352-01-8]
MF: $C_{17}H_{19}FN_4O_2S$ **FW:** 362.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: Selectively inhibits checkpoint kinases Chk1 and Chk2 (IC_{50}s = 5 nM); abrogates DNA damage-induced S and G_2 checkpoints (EC_{50} = 10 nM) and potentiates the efficacy of gemcitabine and topotecan by modulating downstream checkpoint pathway proteins

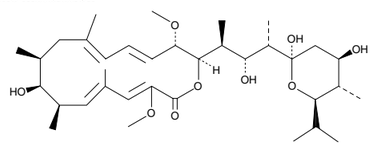
1 mg
5 mg
10 mg
25 mg



Bafilomycin A_1 11038

[88899-55-2] NSC 381866
MF: $C_{35}H_{58}O_9$ **FW:** 622.8 **Purity:** ≥98%
A crystalline solid **Stability:** ≥1 year at -20°C
Summary: A selective, reversible inhibitor of vacuolar H^+ ATPases (V-ATPases), blocking these proton pumps in mammalian, plant, or fungal cells with an IC_{50} value in the 4-400 nM range; also inhibits autophagy by preventing vacuolar acidification necessary for autophagosome maturation

100 µg
1 mg



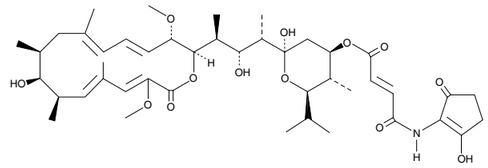
PI3K/Akt Pathway Inhibitors

Item No.	Item Name	Target	Inhibitory Concentration
13622	AS-041164	PI3Kγ	IC_{50} = 70 nM
10009052	AS-252424	PI3Kγ	IC_{50} = 30 nM
10010175	AS-604850	PI3Kγ	IC_{50} = 0.25 µM
10007707	AS-605240	PI3Kγ	IC_{50} = 8 nM
9000980	AS-605240 (potassium salt)	PI3Kγ	IC_{50} = 8 nM
10009078	CAY10505	PI3Kγ	IC_{50} = 30 nM
10010233	CAY10567	Akt1	IC_{50} = ~12.5 µM
13838	CAY10626	PI3Kα mTOR	IC_{50} = 0.9 nM IC_{50} = 0.6 nM
11569	GSK 1059615	PI3Kα	IC_{50} = 2 nM
11811	INK128	TORC1/2	
70920	LY294002	PI3K	IC_{50} = 1.4 µM
13242	3-Methyladenine	PI3K	
10010236	ML-9	PKB/Akt	IC_{50} = 10-50 µM in rat primary adipocytes
10565	NVP-BEZ235	PI3K/mTOR	Inhibits PI3K isoforms and mutants with low nanomolar IC_{50} values
15017	PF-04691502	PI3Kα PI3Kβ PI3Kδ PI3Kγ mTOR	K_i = 1.8 nM K_i = 2.1 nM K_i = 1.6 nM K_i = 1.9 nM K_i = 16 nM
10009209	PI-103	DNA-PK p110α mTORC1 PI3-KC2β p110δ mTORC2 p110β p110γ	IC_{50} = 2 nM IC_{50} = 8 nM IC_{50} = 20 nM IC_{50} = 26 nM IC_{50} = 48 nM IC_{50} = 83 nM IC_{50} = 88 nM IC_{50} = 150 nM
10010177	PI3-Kinase α Inhibitor 2	PI3Kα	IC_{50} = 2 nM
10009210	PIK-75 (hydrochloride)	p110α	IC_{50} = 5.8 nM
10010749	PIK-90	PI3Kα PI3Kβ PI3Kγ PI3Kδ	IC_{50} = 11 nM IC_{50} = 350 nM IC_{50} = 18 nM IC_{50} = 58 nM
10728	PIT-1	Inhibits PIP_3/Akt PH domain binding	IC_{50} = 31 µM
10727	3,5-dimethyl PIT-1	Inhibits PIP_3/Akt PH domain binding	IC_{50} = 27 µM
13643	PP242	Active site of mTORC1 and mTORC2	IC_{50} = 8 nM
13346	Rapamycin	mTORC1	
10876	SC-66	Akt	
11029	SMI-4a	mTORC1	IC_{50}s ranging from 0.8 to 40 µM
11590	Temsirolimus	mTOR	Potency similar to rapamycin
10007349	TGX-221	p110β	IC_{50} = 50 nM in platelets
10997	Torin 1	mTORC1 mTORC2	IC_{50} = 2 nM IC_{50} = 10 nM
14185	Torin 2	mTOR	EC_{50} = 0.3 nM
10010237	Triciribine	Akt	IC_{50} = ~5-10 µM in Akt-overexpressing human cancer cell lines
10010591	Wortmannin	PI3K	IC_{50} = 1-10 nM
13812	17β-hydroxy Wortmannin	PI3K mTOR	IC_{50} = 2.7 nM IC_{50} = 193 nM
13604	WYE-354	PI3K mTOR	IC_{50} = 1,026 nM IC_{50} = 4.3 nM

Bafilomycin B_1 14005

[88899-56-3] Setamycin
MF: $C_{44}H_{65}NO_{13}$ **FW:** 816.0 **Purity:** ≥97%
A crystalline solid **Stability:** ≥1 year at -20°C
Summary: A selective, reversible inhibitor of V-ATPases in mammalian, plant, or fungal cells with an IC_{50} value in the 4-400 nM range; at 100 nM, the related bafilomycin A_1 blocks V-ATPase-mediated acidification of lysosomes during autophagy, preventing protein degradation

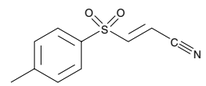
100 µg
1 mg
5 mg



BAY-11-7082 10010266

[19542-67-7]
MF: $C_{10}H_9NO_2S$ **FW:** 207.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A selective and irreversible inhibitor of NF-κB activation that blocks TNF-α-induced phosphorylation of IκB-α without affecting constitutive IκB-α phosphorylation; inhibits the TNF-α-induced surface expression of adhesion molecules intracellular cell adhesion molecule-1, vascular cell adhesion molecule-1, and E-selectin in human endothelial cells (IC_{50} = 5-10 µM)

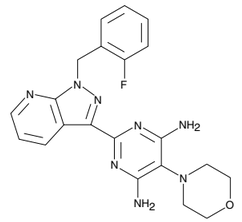
5 mg
10 mg
25 mg
50 mg



BAY-41-8543 10011131

[256498-66-5]
MF: $C_{21}H_{21}FN_8O$ **FW:** 420.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A stimulator of sGC, increasing the activity of recombinant sGC dose-dependently, from 0.1 nM to 100 µM, up to 92-fold; *in vitro*, relaxes vessels and inhibits platelet aggregation at nM concentrations; *in vivo*, decreases blood pressure dose-dependently, prolongs bleeding time, and reduces thrombosis

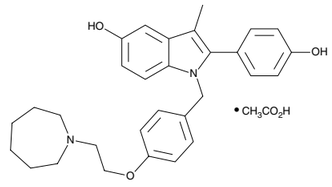
1 mg
5 mg
10 mg
25 mg



Bazedoxifene acetate 15005

[198181-33-3] TSE 424
MF: $C_{30}H_{34}N_2O_3 \bullet C_2H_4O_2$ **FW:** 530.7 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An indole-based SERM that binds to both ERα (IC_{50} = 26 nM)and ERβ (IC_{50} = 99 nM); antagonizes 17β-estradiol-dependent and hormone-independent growth of breast cancer cell proliferation (80% reduction with 10 nM) in a manner related to cell cycle arrest and downregulation of cyclin D1 and ERα

5 mg
10 mg
25 mg
50 mg

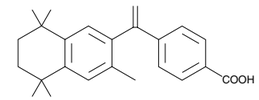


NOTE: Sold for research purposes under agreement from Pfizer Inc.

Bexarotene 11571

[153559-49-0] LG 100069, LGD 1069, Ro 26-4455, SR 11247, Targretin
MF: $C_{24}H_{48}O_2$ **FW:** 348.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A high-affinity ligand for RXRs (EC_{50} = 28, 25, and 20 nM for RXRα, β, and γ, respectively); inhibits cell cycle progression, induces apoptosis, and blocks angiogenesis and metastasis; stimulates clearance of soluble Aβ, reduces plaque area, and reverses deficits related to Alzheimer's disease in mice

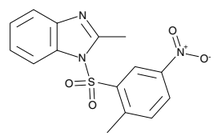
5 mg
10 mg
50 mg



BI6015 12032

[93987-29-2]
MF: $C_{15}H_{13}N_3O_4S$ **FW:** 331.3 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A small molecule antagonist of HNF4α that at 20 µM reduces endogenous insulin gene expression by as much as 50-fold in T6PNE cells; induces hepatic steatosis *in vivo* and is cyctotoxic to human hepatocellular carcinoma cell lines

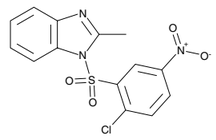
5 mg
10 mg
50 mg



BIM5078 12031

[337506-43-1]
MF: $C_{14}H_{10}ClN_3O_4S$ **FW:** 351.8 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An HNF4α antagonist that can repress the expression of known HNF4α target genes, inhibiting endogenous insulin expression *in vitro* (IC_{50} = 930 nM)

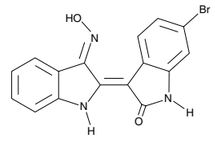
5 mg
10 mg
25 mg
50 mg



BIO 13123

[667463-62-9] 6-Bromoindirubin-3'-oxime, GSK 3 IX, MLS 2052
MF: $C_{16}H_{10}BrN_3O_2$ **FW:** 356.2 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A cell-permeable *bis*-indolo (indirubin) compound that acts as a highly potent, selective, reversible, and ATP-competitive inhibitor of GSK3α/β (IC_{50} = 5 nM); inhibition of GSK activates the Wnt signaling pathway and sustains pluripotency in human and mouse ESCs; maintains self-renewal in human and mouse ESCs as well as induces the differentiation of neonatal cardiomyocytes

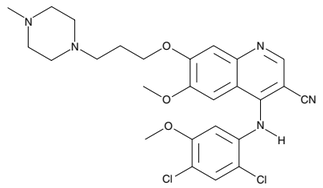
1 mg
5 mg
10 mg
25 mg



Bosutinib 12030

[380843-75-4] SKI-606
MF: $C_{26}H_{29}Cl_2N_5O_3$ **FW:** 530.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: Best known as a potent dual inhibitor of c-Src and Abl (IC_{50} = 1.2 and 1.0 nM, respectively); can be effective in regulating tumor growth and differentiation; also inhibits other members of the Src and TEC families and certain other kinases at nanomolar concentrations

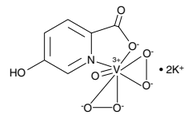
5 mg
10 mg
50 mg
100 mg



bpV(HOpic) (potassium salt) 14433

[722494-26-0] Bisperoxovanadium(HOpic)
MF: $C_6H_4NO_8V$ • 2K **FW:** 347.2 **Purity:** ≥95%
A yellow crystalline solid **Stability:** ≥2 years at -20°C
Summary: A bpV compound that selectively inhibits PTEN (IC_{50} = 14 nM); also inhibits the vascular endothelial PTP, PTP-β (IC_{50} = 4.9 μM), and PTP-1βB (IC_{50} = 25.3 μM) with reduced potency

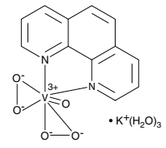
5 mg
25 mg



bpV(phen) (potassium hydrate) 13331

[171202-16-7] Bisperoxovanadium(phen), Potassium Bisperoxo(1,10-phenanthroline) oxovanadate (V)
MF: $C_{12}H_8N_2O_5V$ • $K^+(H_2O)_3$ **FW:** 404.3 **Purity:** ≥99%
A yellow to orange crystalline solid **Stability:** ≥2 years at -20°C
Summary: An inhibitor of several different PTPs, with selectivity for PTEN (IC_{50} = 38 nM); also inhibits PTP-β (IC_{50} = 343 nM), PTP-1β (IC_{50} = 920 nM), and SH2-containing inositol phosphatase; activates the insulin receptor tyrosine kinase and promotes downstream signaling, including activation of PI3-kinase.

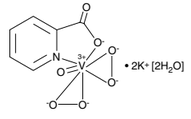
5 mg
25 mg



bpV(pic) (potassium hydrate) 14434

[148556-27-8] Bisperoxovanadium(pic)
MF: $C_6H_4NO_7V$ • 2K $[2H_2O]$ **FW:** 367.3 **Purity:** ≥96%
A yellow crystalline solid **Stability:** ≥2 years at -20°C
Summary: A bisperoxovanadium compound that selectivity inhibits PTEN (IC_{50} = 31 nM); also inhibits the vascular endothelial PTP, PTP-β (IC_{50} = 12.7 μM), and PTP-1βB (IC_{50} = 61 μM) and is known to be an insulin mimetic capable of activating the insulin receptor kinase

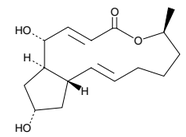
5 mg
25 mg



Brefeldin A 11861

[20350-15-6] Ascotoxin, BFA, Cyanein, Decumbin, Nectrolide, NSC 56310, NSC 89671, NSC 107456, NSC 244390, Synergisidin
MF: $C_{16}H_{24}O_4$ **FW:** 280.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A natural fungal metabolite which reversibly interferes with protein trafficking and secretion mediated by the Golgi apparatus and endoplasmic reticulum; directly and reversibly inhibits Sec7 domain-containing GEFs which are necessary for Arf activation associated with vesicular transport (IC_{50} = ~10 μM)

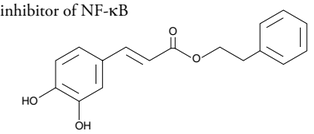
5 mg
10 mg
25 mg



Caffeic Acid phenylethyl ester 70750

[104594-70-9] CAPE, 2-Phenylethyl Caffeate, β-Phenylethyl Caffeate
MF: $C_{17}H_{16}O_4$ **FW:** 284.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥1 year at -20°C
Summary: A potent and specific inhibitor of NF-κB

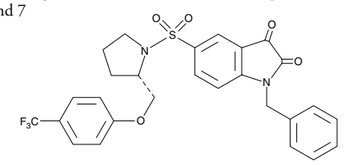
50 mg
100 mg
500 mg
1 g



CAY10406 72510

MF: $C_{27}H_{23}F_3N_2O_5S$ **FW:** 512.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A trifluoromethyl analog of an isatin sulfonamide compound that selectively inhibits caspases 3 and 7

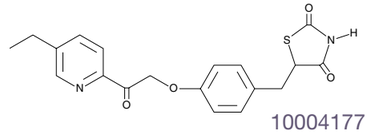
1 mg
5 mg
10 mg
100 mg



CAY10415 71748

[146062-49-9]
MF: $C_{19}H_{18}N_2O_4$ **FW:** 370.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent, antidiabetic drug of the thiazolidinedione structural class that lowers blood glucose leves in obese, hyperglycemic, hyperinsulinemic, and insulin-resistant KKA_y mice at a dose of 100 mg/kg for four days; increases the rate of insulin-stimulated lipogenesis in 3T3-L1 adipocytes in a dose-dependent manner.

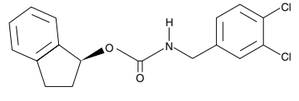
1 mg
5 mg
10 mg
50 mg



CAY10443 10004177

[582314-48-5] (S)-Indan-1-yl 3,4-dichlorobenzylcarbamate
MF: $C_{17}H_{15}Cl_2NO_2$ **FW:** 336.1 **Purity:** ≥98%
A crystalline solid **Stability:** ≥1 year at -20°C
Summary: A pro-apoptotic activator of the apoptosome; activates caspase-3 (EC_{50} = 5 μM) in a cell free, multi-component assay

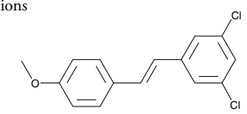
1 mg
5 mg
10 mg
50 mg



CAY10464 10006545

[688348-37-0]
MF: $C_{15}H_{12}Cl_2O$ **FW:** 279.2 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent and selective AhR antagonist with a K_i value of 1.4 nM when tested in rabbit liver cytosol preparations

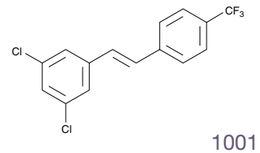
10 mg
25 mg
50 mg
100 mg



CAY10465 10006546

[688348-33-6]
MF: $C_{15}H_9Cl_2F_3$ **FW:** 317.1 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An analog of resveratrol that acts as a potent and selective AhR agonist (K_i = 0.2 nM)

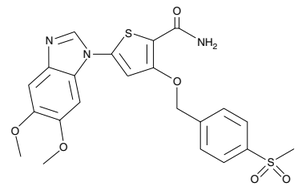
1 mg
5 mg
10 mg
50 mg



CAY10575 10011248

[916985-21-2]
MF: $C_{22}H_{21}N_3O_6S_2$ **FW:** 487.6 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A benzimidazole analog that inhibits IKK-ε with an IC_{50} value of ~15.8 μM

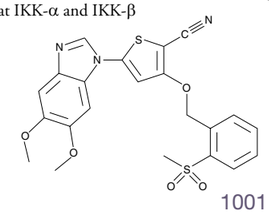
1 mg
5 mg
10 mg
25 mg



CAY10576 10011249

[862812-98-4]
MF: $C_{22}H_{19}N_3O_5S_2$ **FW:** 469.5 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A benzimidazole analog that selectively inhibits IKK-ε with an IC_{50} value of 40 nM and is essentially inactive at IKK-α and IKK-β

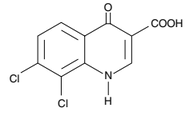
1 mg
5 mg
10 mg
50 mg



CAY10577 10011256

[300675-28-9]
MF: $C_{10}H_5Cl_2NO_3$ **FW:** 258.1 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A CK2 inhibitor with an IC_{50} value of 0.8 μM

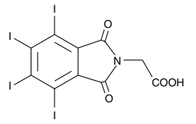
1 mg
5 mg
10 mg
50 mg



CAY10578 10011264

[19231-60-8]
MF: $C_{10}H_3I_4NO_4$ **FW:** 708.8 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent and selective inhibitor of CK2 with an IC_{50} value of 0.3 μM and a K_i value of 0.2 μM

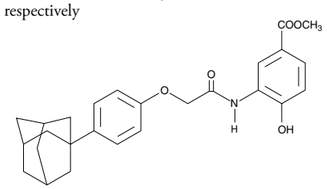
1 mg
5 mg
10 mg
25 mg



CAY10585 10012682

[934593-90-5] Hypoxia Inducible Factor-1α Inhibitor
MF: $C_{26}H_{29}NO_5$ **FW:** 435.5 **Purity:** ≥97%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A novel inhibitor of HIF-1α accumulation and gene transcriptional activity; inhibits HIF-1 transcriptional activity with IC_{50} values of 2.6 and 0.7 μM in human Hep3b and AGS cells, respectively

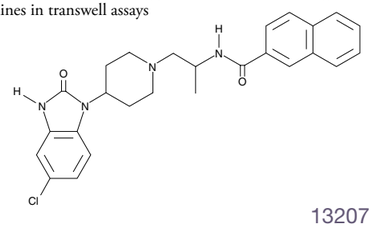
1 mg
5 mg
10 mg
25 mg



CAY10593 13206

VU0155069
MF: $C_{26}H_{27}ClN_4O_2$ **FW:** 463.0 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent and selective inhibitor of PLD_1, both *in vitro* (IC_{50} = 46 nM) and in cells (IC_{50} = 11 nM); also effective as a PLD_2 inhibitor at higher concentrations (IC_{50} = 933 nM *in vitro*; 1,800 nM in cells); strongly inhibits the invasive migration of several breast cancer cell lines in transwell assays

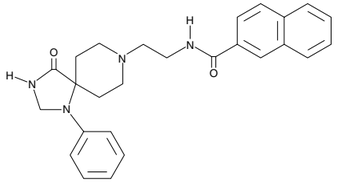
1 mg
5 mg
10 mg
25 mg



CAY10594 13207

[1130067-34-3]
MF: $C_{26}H_{28}N_4O_2$ **FW:** 428.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent PLD_2 inhibitor, both *in vitro* (IC_{50} = 140 nM) and in cells (IC_{50} = 110 nM); also effective as a PLD_1 inhibitor at higher concentrations (IC_{50} = 5.1 μM *in vitro*, 1.0 μM in cells); strongly inhibits the invasive migration of breast cancer cells in transwell assays

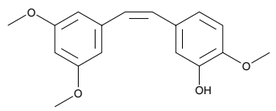
1 mg
5 mg
10 mg
25 mg



CAY10616 13291

[586410-08-4]
MF: $C_{17}H_{18}O_4$ **FW:** 286.3 **Purity:** ≥98%
A solution in methyl acetate **Stability:** ≥1 year at -20°C
Summary: An analog of resveratrol which potently induces apoptosis in HL-60 cells (IC_{50} = 40 nM *versus* 50 µM for resveratrol); induces apoptosis (IC_{50} = 30 nM) in HL-60R, a multidrug-resistant cell line derived from HL-60

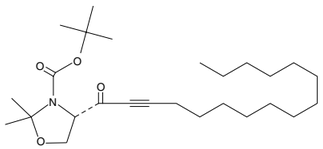
1 mg
5 mg
10 mg
25 mg



CAY10621 13371

[120005-55-2] SKI 5C, SPHK 1 Inhibitor 5C
MF: $C_{26}H_{45}NO_4$ **FW:** 435.6 **Purity:** ≥98%
A solution in methyl acetate **Stability:** ≥1 year at -20°C
Summary: A selective inhibitor of SPHK 1, both *in vitro* (IC_{50} = 3.3 µM) and in U937 cells overexpressing human SPHK 1 (70% inhibition at 5 µM); has no inhibitory effect on SPHK 2 either *in vitro* or in cells

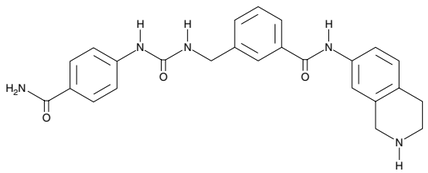
1 mg
5 mg
10 mg
25 mg



CAY10622 13687

[1038549-25-5]
MF: $C_{25}H_{25}N_5O_3$ **FW:** 443.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent inhibitor of ROCK-I and ROCK-II kinases (IC_{50}s = 6 and 4 nM, respectively)

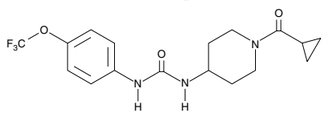
1 mg
5 mg
10 mg
25 mg



CAY10640 10642

[1208549-68-1] sEHi, Soluble Epoxide Hydrolase Inhibitor
MF: $C_{17}H_{20}F_3N_3O_3$ **FW:** 371.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: Inhibits recombinant human and mouse sEH (IC_{50}s both = 0.4 nM) and demonstrates a 1,000-fold increase in potency compared to morphine in reducing hyperalgesia in an *in vivo* carrageenan-induced inflammatory pain model

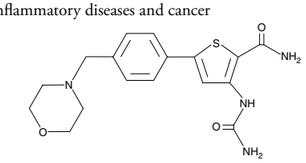
1 mg
5 mg
10 mg



CAY10657 11140

[494772-86-0]
MF: $C_{17}H_{20}N_4O_3S$ **FW:** 360.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A thiophene carboxamide derivative proposed to inhibit IKK-2; likely to be useful in the treatment of inflammatory diseases and cancer

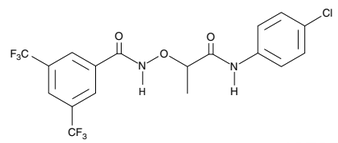
1 mg
5 mg
10 mg



CCG-1423 10010350

[285986-88-1]
MF: $C_{18}H_{13}ClF_6N_2O_3$ **FW:** 454.8 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A novel, specific inhibitor of Rho pathway-mediated signaling and activation of SRF transcription; inhibits DNA synthesis, proliferation, and invasion of Rho-overexpressing cell lines at nanomolar to low micromolar concentrations

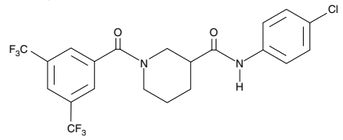
5 mg
10 mg
25 mg
50 mg



CCG-100602 10787

[1207113-88-9]
MF: $C_{21}H_{17}ClF_6N_2O_2$ **FW:** 478.8 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: Inhibits RhoA/C-mediated, SRF-driven luciferase expression in PC-3 prostate cancer cells with an IC_{50} value of 9.8 µM

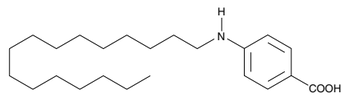
5 mg
10 mg
25 mg
50 mg



Cetaben 10007171

[55986-43-1] Hexadecylamino-p-amino Benzoic Acid
MF: $C_{23}H_{39}NO_2$ **FW:** 361.6 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A unique, PPARα-independent peroxisome proliferator with hypolipidemic activity characterized by reduction in serum triglyceride and cholesterol

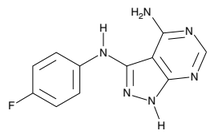
5 mg
10 mg
50 mg
100 mg



CGP 57380 13322

[522629-08-9] MNK1 Inhibitor
MF: $C_{11}H_9FN_6$ **FW:** 244.2 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A selective inhibitor of MNK1 *in vitro* (IC_{50} = 2.2 µM), with no inhibitory activity against p38, JNK1, ERK1/2, PKC, or Src-like kinases; blocks the phosphorylation of eIF4E in response to TNF-α, arsenite, anisomycin, PMA, or fetal calf serum in 293 cells (IC_{50} = 3 µM)

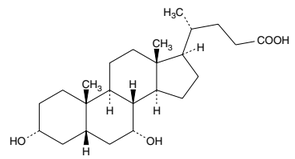
1 mg
5 mg
10 mg
25 mg



Chenodeoxycholic Acid 10011286

[474-25-9] Anthropodeoxycholic Acid, CDCA, Fluibil, Hekbilin, Kebilis, Ulmenide
MF: $C_{24}H_{40}O_4$ **FW:** 392.6 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A bile acid and FXR ligand (EC_{50} = 13-34 µM) that is a key regulator of cholesterol homeostasis; exhibits toxicity that is linked to increased glutathione and increased oxidative stress; excess CDCA contributes to liver and intestinal cancers

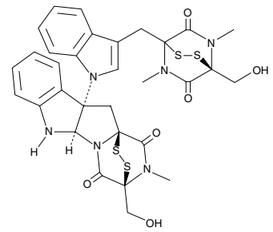
1 g
5 g
10 g
25 g



Chetomin 14437

[1403-36-7] NSC 289491
MF: $C_{31}H_{30}N_6O_6S_4$ **FW:** 710.9 **Purity:** ≥98%
An off-white to fawn solid **Stability:** ≥1 year at -20°C
Summary: A natural product which acts as a small molecule inhibitor of HIF signaling, disrupting the binding of HIF-1α and HIF-2α to p300 at low nanomolar concentrations; effectively attenuates the HIF pathway both in cells and *in vivo*, in mice

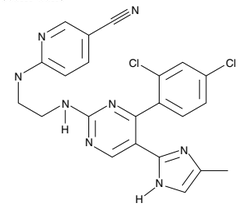
1 mg
5 mg



CHIR99021 13122

[252917-06-9] CT 99021
MF: $C_{22}H_{18}Cl_2N_8$ **FW:** 465.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An aminopyrimidine derivative that inhibits GSK3α and GSK3β (IC_{50}s = 10 and 6.7 nM, respectively); activates glycogen synthesis in CHO-IR cells (EC_{50} = 0.8 µM) and in isolated type 1 diabetic rat skeletal muscle; has been shown to promote self-renewal of embryonic stem cells

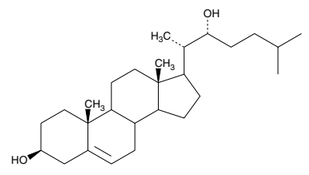
1 mg
5 mg
10 mg



22(R)-hydroxy Cholesterol 89355

[17954-98-2] Narthesterol
MF: $C_{27}H_{46}O_2$ **FW:** 402.7 **Purity:** ≥98%
A crystalline solid **Stability:** ≥1 year at -20°C
Summary: An endogenous agonist for LXRα (EC_{50} = 325 nM) that can induce the expression of the ABCA1 reverse cholesterol transporter to inhibit the overall absorption of cholesterol; used as a substrate to monitor cholesterol transport or as an endogenous positive control for testing LXR agonists

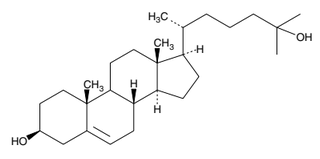
1 mg
5 mg
10 mg



25-hydroxy Cholesterol 11097

[2140-46-7]
MF: $C_{27}H_{46}O_2$ **FW:** 402.7 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A side-chain substituted oxysterol derived from dietary cholesterol that inhibits the cleavage of SREBPs; has been implicated in a variety of metabolic events including cholesterol homeostasis and atherosclerosis as well as antitumor and immunomodulating activities

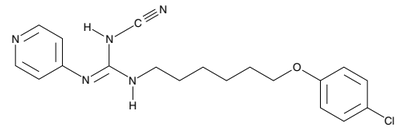
5 mg
10 mg
25 mg
100 mg



CHS-828 11021

[200484-11-3] GMX 1778
MF: $C_{19}H_{22}ClN_5O$ **FW:** 371.9 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An inhibitor of nicotinamide phosphoribosyltransferase and NF-κB pathway activity; potent cytotoxic effects in human breast (IC_{50} = 7.3 nM) and lung cancer (IC_{50} = 0.5 nM) cells lines; inhibits the growth of MCF-7 breast cancer tumors and induces regression of NYH small cell lung cancer xenografts in nude mice at 20-50 mg/kg/day

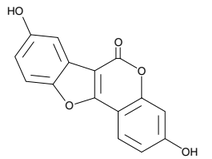
5 mg
25 mg



Coumestrol 11730

[479-13-0] NSC 22842
MF: $C_{15}H_8O_5$ **FW:** 268.2 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A phytoestrogen that competitively (*vs.* 17β-estradiol) binds the ERs (ERα (IC_{50} = 11 nM) and ERβ (IC_{50} = 2 nM)) and can induce ER-dependent gene expression in isolated cells; a weak antagonist of pregnane X receptor (IC_{50} = 12 µM)

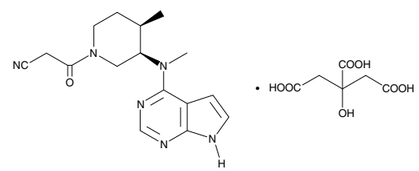
1 mg
5 mg
10 mg



CP 690,550 11598

[540737-29-9] Tofacitinib citrate
MF: $C_{16}H_{20}N_6O \bullet C_6H_8O_7$ **FW:** 504.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent, cell-permeable inhibitor of all JAK isoforms (IC_{50} = 6.1, 12, and 8.0 nM for JAK1, JAK2, and JAK3, respectively); useful in ameliorating inflammatory or autoimmune components of a host of diseases

5 mg
10 mg
25 mg
50 mg

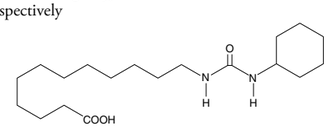


NOTE: Sold for research purposes under agreement from Pfizer Inc.

CUDA 10007923

[479413-68-8]
MF: $C_{19}H_{36}N_2O_3$ **FW:** 340.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An inhibitor of sEH exhibiting IC_{50} values of 11.1 and 112 nM for the mouse and human enzymes, respectively

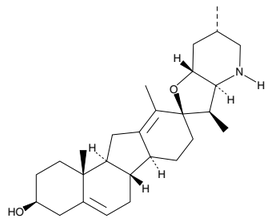
5 mg
10 mg
25 mg
50 mg



Cyclopamine 11321

[4449-51-8] 11-Deoxojervine, Jervine
MF: $C_{27}H_{41}NO_2$ **FW:** 411.6 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A natural steroidal alkaloid that inhibits signaling through the Hh pathway at the level of the pathway activator Smo; inhibits Hh-dependent expression of Pax7 with an IC_{50} value of 24 nM; has potential applications in the treatment of cancer

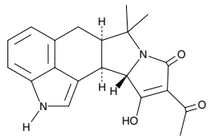
1 mg
5 mg
10 mg



Cyclopiazonic Acid 11326

[18172-33-3] NSC 117181
MF: $C_{20}H_{20}N_2O_3$ **FW:** 336.4 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A mycotoxin that specifically and reversibly inhibits sarco-endoplasmic reticulum Ca^{2+}-ATPases (SERCA; IC_{50} = 0.6 µM); effectively inhibits SERCA in intact tissue, in smooth muscle and endothelium, as well as in isolated cells

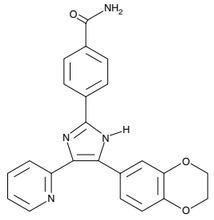
1 mg
5 mg
10 mg



D 4476 13305

[301836-43-1] Casein Kinase 1 Inhibitor
MF: $C_{23}H_{18}N_4O_8$ **FW:** 398.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A cell-permeant inhibitor of CK1; (IC_{50} = 200 nM from *S. pombe*, 300 nM for CK1δ); only weakly affects the activities of a panel of kinases tested

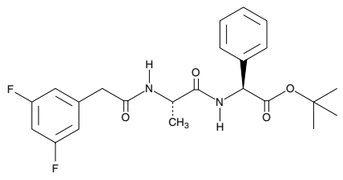
1 mg
5 mg
10 mg
50 mg



DAPT 13197

[208255-80-5] GSI-IX
MF: $C_{23}H_{26}F_2N_2O_4$ **FW:** 432.5 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An inhibitor of γ-secretase, blocking the production of total Aβ in human primary neuronal cultures with an IC_{50} value of 115 nM and Aβ42 with an IC_{50} value of 200 nM; reduces brain levels of Aβ *in vivo* when given orally; indirectly inhibits Notch, affecting cell signaling and cell differentiation

5 mg
10 mg
25 mg
50 mg



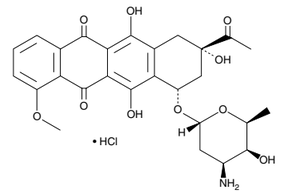
Cell-division Cycle Inhibitors

Item No.	Product Name	Target	Inhibitory Concentration
14428	Alsterpaullone	CDK1/cyclin B CDK2/cyclin A CDK2/cyclin E CDK5/p25 GSK-3α/β	IC_{50} = 35 nM IC_{50} = 15 nM IC_{50} = 200 nM IC_{50} = 40 nM IC_{50} = 4 nM
10010301	CAY10554	CDK5 CDK2	IC_{50} = 64 nM IC_{50} = 98 nM
18218	CAY10572	Cdc7 kinase CDK9	IC_{50} = 10 nM IC_{50} = 34 nM
10011247	CAY10574	CDK9 CDK2-cyclin E	IC_{50} = 0.35 µM IC_{50} = 20 µM
14006	(R)-CR8	CDK1 CDK2 CDK5 CDK9 CK1δ/ε GSK-3α/β	IC_{50} = 0.09 µM IC_{50} = 0.072-0.041 µM IC_{50} = 11 µM IC_{50} = 0.18 µM IC_{50} = 0.40 µM IC_{50} = 12 µM
10010302	DRB	CK2 CDK7 CDK8 CDK9	IC_{50} = 4-10 µM IC_{50} = ~20 µM IC_{50} = ~20 µM IC_{50} = 3 µM
10010239	Kenpaullone	CDKs GSK3β	
13303	NSC 663284	Cdc25A Cdc25B2 Cdc25C	IC_{50} = 29 nM IC_{50} = 95 nM IC_{50} = 89 nM
13317	NU 6102	CDK1 CDK2	K_i = 9 nM K_i = 6 nM
10010240	Olomoucine	CDC2/cyclin B CDK2/cycln A CDK/p35 kinase	IC_{50} = 7 µM IC_{50} = 7 µM IC_{50} = 7 µM
13325	Iso-Olomoucine	CDK5	IC_{50} = ~37 µM
14579	Purvalanol A	Cdc2/cyclin B CDK2/cyclin A CDK2/cyclin E CDK4/cyclin D1 CDK5-p35	IC_{50} = 4 nM IC_{50} = 70 nM IC_{50} = 35 nM IC_{50} = 850 nM IC_{50} = 75 nM
10009569	(R)-Roscovitine	CDK2/cyclin E CDK7/cyclin H CDK5/p35 Cdc/cyclin B	IC_{50} = 0.1 µM IC_{50} = 0.49 µM IC_{50} = 0.16 µM IC_{50} = 0.65 µM
14187	S14161	Cyclins D1-D3	5-10 µM

Daunorubicin (hydrochloride) 14159

[23541-50-6] NDC 0082-4155, Ondena, RP 13057
MF: $C_{27}H_{29}NO_{10}$ • HCl **FW:** 564.0 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An antitumor antibiotic that induces apoptosis in mature monocytic U937 and myelocytic HL-60 acute myeloid leukemia cells at 0.2-1 µM; triggers a ROS-dependent sphingomyelin-ceramide pathway that activates the MEKK1-SEK1-JNK

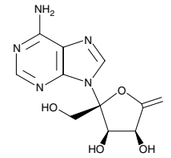
5 mg
10 mg
50 mg
100 mg



Decoyinine 13851

[2004-04-8] Angustmycin A
MF: $C_{11}H_{13}N_5O_4$ **FW:** 279.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥1 year at -20°C
Summary: A nucleoside analog from bacteria which acts as a selective GMP synthetase inhibitor (K_i = 50 µM); modulates gene expression related to sporulation in bacteria and mycelium formation in *Streptomyces*

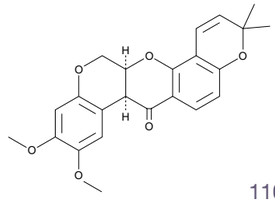
1 mg
5 mg



(-)-Deguelin 10010706

[522-17-8] (-)-cis-Deguelin
MF: $C_{23}H_{22}O_6$ **FW:** 394.1 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A rotenoid compound with chemopreventive and chemosensitizing effects in models of skin, mammary, colon, and lung carcinogenesis; inhibits cell growth (IC_{50} = $<10^{-8}$ M), blocks PI3K/Akt signaling, suppresses COX-2 expression, and induces apoptosis of premalignant and squamous HBE cells without affecting normal HBE cells

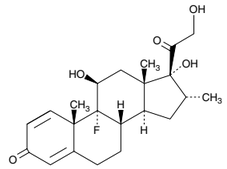
5 mg
10 mg
25 mg
50 mg



Dexamethasone 11015

[50-02-2] MK 125, NSC 34521
MF: $C_{22}H_{29}FO_5$ **FW:** 392.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A synthetic glucocorticoid that binds the human glucocorticoid receptor with a higher affinity than a natural ligand, cortisol (K_d = 5 *vs.* 17 nM, respectively); has anti-inflammatory effects

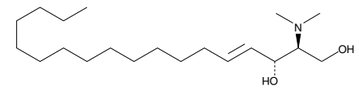
500 mg
1 g
5 g



N,N-Dimethylsphingosine 62575

[119567-63-4]
MF: $C_{20}H_{41}NO_2$ **FW:** 327.6 **Purity:** ≥98%
A solution in ethanol **Stability:** ≥1 year at -20°C
Summary: An inhibitor of SPHK and a natural metabolite of sphingosine in some cancer cell lines and tissues; inhibits SPHK from U937 cells with a K_i value of 3.1 µM

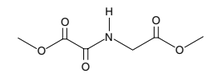
5 mg
10 mg
25 mg
50 mg



DMOG 71210

[89464-63-1] Dimethyloxallyl Glycine
MF: $C_6H_9NO_5$ **FW:** 175.1 **Purity:** ≥98%
A crystalline solid **Stability:** ≥1 year at -20°C
Summary: A cell permeable, competitive inhibitor of HIF-α prolyl hydroxylase; stabilizes HIF-1α expression at normal oxygen tensions in cultured cells at concentrations between 0.1 and 1 mM

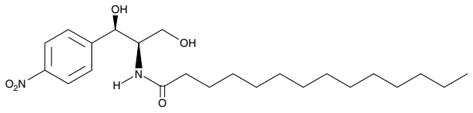
10 mg
50 mg
100 mg
500 mg



D-NMAPPD 10006305

[35922-06-6] (1R,2R)-B13, CAY10466
MF: $C_{23}H_{38}N_2O_5$ **FW:** 422.6 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent ceramidase inhibitor that induces apoptosis in human colorectal cancer, keratinocyte, and melanoma cell lines; produces approximately 50% cell non-viability at 10 µM and >80% cell death at 100 µM

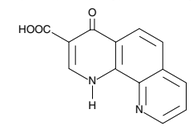
1 mg
5 mg
10 mg
50 mg



1,4-DPCA 71220

[331830-20-7] 1,4-dihydrophenonthrolin-4-one-3-Carboxylic Acid
MF: $C_{13}H_8N_2O_3$ **FW:** 240.2 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A competitive inhibitor of prolyl 4-hydroxylase (IC_{50} = 2.4-3.6 µM)

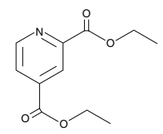
5 mg
10 mg
25 mg
50 mg



2,4-DPD 71200

[41438-38-4] 2,4-Diethylpyridine dicarboxylate
MF: $C_{11}H_{13}NO_4$ **FW:** 223.2 **Purity:** ≥98%
A solution in ethanol **Stability:** ≥1 year at -20°C
Summary: A cell permeable, competitive inhibitor of HIF-PH with effective concentrations in the low µM range

10 mg
25 mg
50 mg
100 mg



Considering cAMP's Complexity

by [Thomas G. Brock, Ph.D.]

Considering cAMP's Complexity

The sage Lao-tzu noted that 'a journey of a thousand miles begins with a single step'. Few scientists could have anticipated the twists and turns that their journeys through science would take when they took their first step. The simplicity inherent in a single step contrasts vividly with the complexity of reality, which helps explain the appeal of Lao-tzu's viewpoint. So it is with cell signaling. It's appealing to declare that activation of β_2-adrenergic receptors elevates cyclic AMP (cAMP) as a first step toward evoking downstream effects. However, the details of how cAMP works are intricate and, as a result, much more interesting than a single second messenger step. This article touches on some of the factors that interplay with the actions of cAMP.

The Basics

The synthesis of cAMP as a second messenger, from ATP, is mediated by adenylate cyclase (AC), which in turn is modulated by G protein-coupled receptors (GPCRs; Figure 1). AC is activated by GPCRs which contain the $G\alpha_s$ subunit and inhibited by those with the $G\alpha_i$ subunit. Of the multiple isoforms of AC in humans, there are three (AC5-7) which are inhibitable by calcium and two isoforms (AC1, AC8) which are stimulated by calcium/calmodulin. The inhibition of cAMP production by $G\alpha_i$–coupled receptors or by calcium is relevant for both reducing basal cAMP production in unstimulated cells (which can be appreciable) and blocking the increased cAMP generation where AC activity is stimulated by $G\alpha_s$-coupled receptors or by calmodulin.

An important pathway that is cAMP-dependent involves the membrane-associated *E*xchange *P*roteins *A*ctivated by *c*AMP (Epac), Epac-1 and Epac-2 (Figure 1). These are two of several guanine nucleotide exchange factors (GEFs) that target the Ras GTPase homologs Rap1 and Rap2. The Rap proteins are activated when bound GDP is replaced with GTP by a GEF, like Epac. Hydrolysis of GTP to GDP *in situ* inactivates Rap. The cAMP-Epac-Rap pathways are involved in regulating a variety of different cell-specific processes, ranging from cell motility to gene expression.

The prototypical pathway activated by cAMP involves protein kinase A (PKA). In resting cells, PKA exists has a tetramer of two regulatory subunits holding two catalytic subunits (Cα) in an inactive state. The classical model posits that the association of cAMP with the regulatory subunits induces dissociation of the tetramer, allowing the free and active catalytic subunits of the kinase to phosphorylate target proteins. Targets of Cα may be either cytoplasmic or intranuclear, as these subunits are small enough to diffuse through nuclear pores. In humans, there are three genes encoding PKA catalytic subunits and

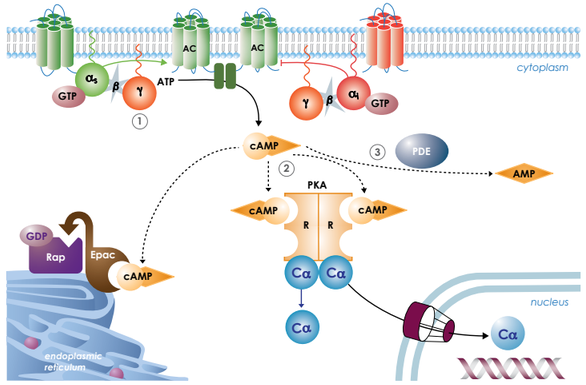


Figure 1. Signaling through the second messenger cAMP

four encoding regulatory subunits, so the regulation of expression and protein function can be complex. Moreover, there are at least three genes that encode inhibitors of PKA, proteins that bind PKA catalytic subunits, promote their export from the nucleus, and impair their kinase function.

PKA phosphorylates a broad spectrum of target proteins. Recent approaches for identifying these substrates include reverse in-gel kinase assays,[1] evolutionary proteomic conservation,[2] and high-throughput prediction.[3] A PKA consensus motif, RRXS/T, has been identified, although the shorter motif of RXS/T is also targeted by Akt and PKC. The majority of these hundreds of targets are involved in an 'immediate' response to a transient rise in cAMP levels. However, Montminy and colleagues described a cAMP-responsive element in the rat somatostatin gene in 1986, leading to the identification of the cAMP response element-binding proteins (CREBs).[4] A basic region and leucine zipper (bZIP) domain on CREB permits both specific DNA binding and dimerization (Figure 2). CREB-mediated changes in gene expression have been implicated in such diverse processes as reproduction, learning, memory, immune response, differentiation of adipose tissues, and circadian rhythm. CREB can be phosphorylated, and thus modulated, by several kinases in addition to PKA, including CaMK IV, Akt, Rsk2, Msk, and MAPKAPK2.[5] CREB thus represents a convergence point of signals from such varied cellular agonists as neurotransmitters, cytokines, bioactive lipids, growth factors, and stress.

Phosphodiesterases

As noted in Figure 1, cAMP is metabolized to AMP by phosphodiesterases (PDEs). There are several PDE isoforms, and some are cAMP-specific, some target cGMP only, and some break down both. Inhibitors of PDEs can prolong physiological processes mediated by cyclic nucleotides by delaying their degradation. As the different PDEs have different roles, inhibitors of specific PDEs are clinically important. Inhibitors of PDE4, the major cAMP-metabolizing isoform in immune cells, are used in the treatment of asthma, allergic diseases and inflammation. Some of the better-known PDE4-selective inhibitors are rolipram, cilomilast, and roflumilast, the latter being approved for treating chronic obstructive pulmonary disease. Sildenafil, the active ingredient in Viagra, blocks the cGMP-selective PDE5, prolonging NO-induced/mediated vasodilation which is helpful in treating erectile dysfunction and pulmonary arterial hypertension. Additional PDE-selective inhibitors have been developed, but their movement to market has been limited.[6] In the laboratory, the nonselective PDE inhibitor IBMX is commonly used to allow prolonged signaling through cAMP and cGMP, facilitating the detection of short-term signaling involving these second messengers.

A-Kinase Anchoring Proteins

Please note that the presentation of cAMP signaling as given in Figure 1 is merely an amalgam of a multitude of figures developed for teaching purposes. Technically, such a diagram might best be described as an 'exploded view', designed to show the working parts without indicating their direct interactions. In fact, there is a growing understanding that many signaling pathways, including several of those that involve cAMP, rely on intimate linkages between all components. Central to this concept are the A-kinase anchoring proteins (AKAPs). AKAPs act as platforms for PKA action: AKAPs can bind PKA as well as PKA substrates, other kinases, PDEs, and phosphatases. This allows better regulation of the phosphorylation and dephosphorylation of target proteins.

One example involves the suppression of CD4 signaling in regulatory T cells (Tregs) by prostaglandin E_2 (PGE_2). PGE_2, through the E prostanoid receptor EP_2, activates adenylate cyclase, cAMP synthesis, and PKA-mediated phosphorylation of the non-receptor tyrosine-protein kinase Csk (Figure 3).[7,8] Both PKA and Csk are anchored at the plasma membrane, close to adenylate cyclase, by membrane-associated proteins, AKAP and PAG. As is always the case, AKAP binds the regulatory subunits of PKA, leaving the catalytic subunits free to dissociate at least temporarily. Csk then phosphorylates Src-family kinases (in this case, Lck), leading to impaired signaling through CD4.[9] Two key elements in this model are PAG and AKAP, which pull signaling components together to create localized signaling.

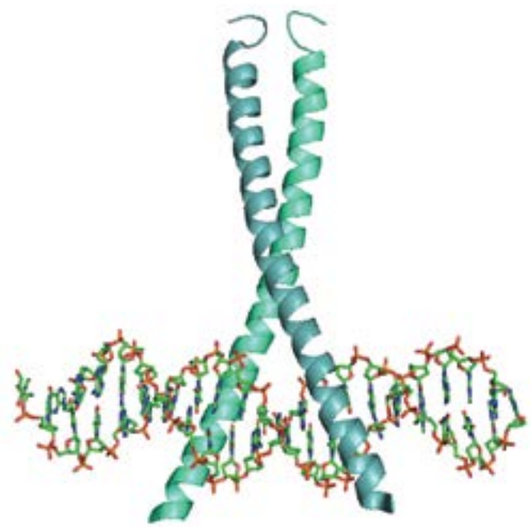


Figure 2. Interaction of the dimerized bZIP domains of 2 CREB proteins at the cAMP response element (from 1DH3.pdb)[13]

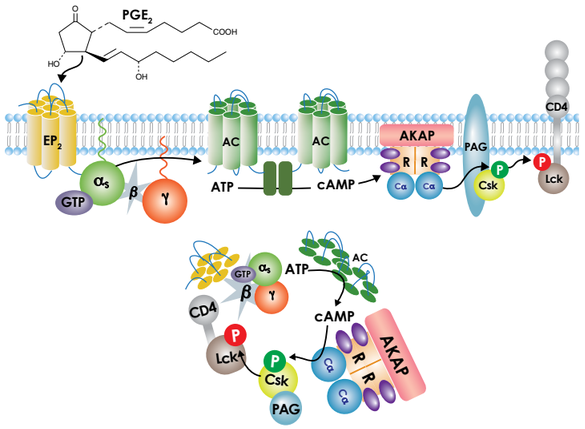


Figure 3. Signaling from PGE_2 through EP_2 and adenylate cyclase (AC) and PKA to Csk-mediated phosphorylation of Lck and inhibition of CD4 can be displayed in either an "exploded view" (upper) or, as a protein complex viewed from above the cell (lower).

Similar clusters of function, centering around AKAPs, abound. For example, calcium channels (TRPC or CCE), co-localize with calcium-activated adenylate cyclase isoforms, with adjacent AKAPs which retain both PKA and PDE4.[10] Transient increases in calcium thus trigger a rise in cAMP, followed directly by hydrolysis of cAMP by PDE4.[11] Hydrolysis of cAMP can occur while it is still bound to the regulatory subunit of PKA. On the flip side, cAMP from adenylate cyclase activated by $G\alpha_s$-coupled receptors (*e.g.*, β_2-adrenergic receptor) can, through AKAP-immobilized PKA, phosphorylate and activate L-type calcium channels. Phosphatase PP2A, co-localized with PKA on the AKAP, dephosphorylates the channel and stops calcium influx.[10] Scott and colleagues have demonstrated that within a given cell type (*e.g.*, cardiomyocytes), diverse AKAPs are positioned throughout the cell, localizing PKA and associated kinases, phosphatases, or PDEs to control PKA signaling both spatially and temporally.[12] The take-home message from these studies, at this point, is that we are only beginning to understand the complexity of PKA signaling at the subcellular level, across various cell types, and in unison with other signaling systems. n

AKAPs act as platforms for PKA action

References

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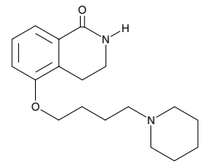
DPQ 14450

[129075-73-6] PARP Inhibitor III
MF: $C_{18}H_{26}N_2O_2$ **FW:** 302.4 **Purity:** ≥99%
A white to off-white solid **Stability:** ≥2 years at 4°C
Summary: A potent inhibitor of PARPs, inhibiting PARP1 with an IC_{50} value of 40 nM; about 10-fold less potent against PARP2

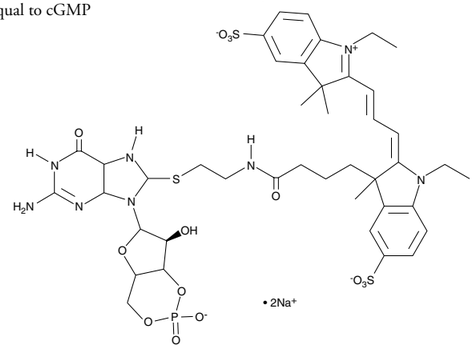
1 mg
5 mg



8-DY547-cGMP 10010109

MF: $C_{42}H_{55}N_8O_{14}PS_3$ • 2Na **FW:** 1,069.1 **Purity:** ≥98%
A solution in ethanol **Stability:** ≥1 year at -20°C
Summary: A fluorescently-labeled cyclic nucleotide to study cyclic nucleotide-gated A2 channel activation; opens the channel in a rapid and reversible manner with efficiency equal to cGMP

50 µg
100 µg



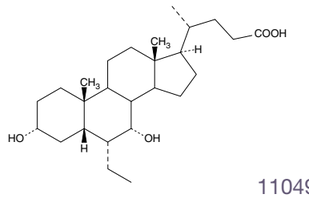
Diacylglycerols

Item No.	Product Name
9000341	1-NBD-decanoyl-2-decanoyl-*sn*-Glycerol
62210	1,2-Didecanoyl-*sn*-glycerol
10008646	1,2-Dihexanoyl-*sn*-glycerol
62225	1,2-Dioctanoyl-*sn*-glycerol
10007863	1,2-Dioleoyl-*rac*-glycerol
62230	1,2-Dioleoyl-*sn*-glycerol
10008648	1,2-Dipalmitoyl-*sn*-glycerol
60920	Hexadecyl Acetyl Glycerol
60930	Hexadecyl Methyl Glycerol
10008650	1-Stearoyl-2-Arachidonoyl-*sn*-Glycerol

6-ECDCA 11031

[459789-99-2] INT 747, Obeticholic Acid
MF: $C_{26}H_{44}O_4$ **FW:** 420.3 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A synthetic bile acid that acts as a potent and selective agonist of FXR (EC_{50} = 99 nM); alters gene expression that results in protection against cholestasis as well as liver fibrosis; promotes the differentiation of adipocytes and enhances insulin signaling in mature adipocytes

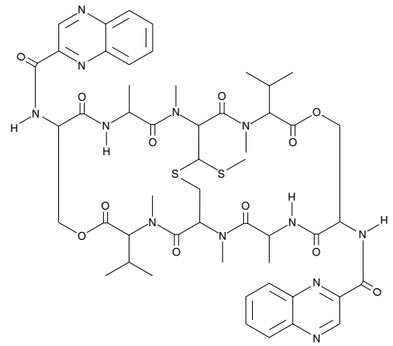
5 mg
25 mg



Echinomycin 11049

[512-64-1] Antibiotic A 6541, NSC 13502, NSC 526417, Quinomycin A, SK 302B
MF: $C_{51}H_{64}N_{12}O_{12}S_2$ **FW:** 1,101.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥1 year at -20°C
Summary: A cell-permeable inhibitor of HIF-1-mediated gene transcription which acts by intercalating into DNA in a sequence-specific manner, blocking the binding of either HIF-1α or HIF-1β to the hypoxia response element; reversibly inhibits hypoxia-induced HIF-1 transcription activity in U215 cells with an EC_{50} value of 1.2 nM

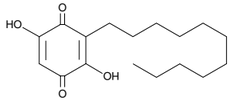
1 mg
5 mg



Embelin 11838

[550-24-3] NSC 91874
MF: $C_{17}H_{26}O_4$ **FW:** 294.4 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A natural benzoquinone which directly binds and inhibits XIAP (IC_{50} = 4.1 µM); blocks growth while activating caspases and promoting apoptosis in cancer cells expressing high levels of XIAP; prevents NF-κB activation by inhibiting IKK; protects against XIAP- and caspase-dependent inflammation

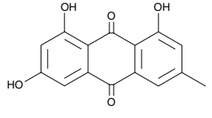
10 mg
50 mg
100 mg



Emodin 13109

[518-82-1] Archin, Frangulic Acid, NSC 408120, NSC 622947, Schuttgelb
MF: $C_{15}H_{10}O_5$ **FW:** 270.2 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A naturally-occurring anthraquinone with diverse effects, including the suppression of inflammation, dyslipidemia, and cancer; directly and selectively inhibits CK2 (IC_{50} = 0.89 µM) and the COP9 signalosome; acts as a phytoestrogen, blocking 17β-estradiol binding to ER with K_i values of 0.77 and 1.5 µM for ERα and ERβ, respectively

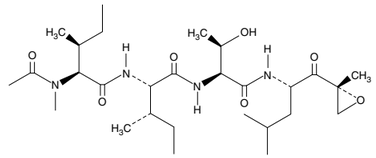
25 mg
50 mg
100 mg



Epoxomicin 10007806

[134381-21-8] BU 4061T
MF: $C_{28}H_{50}N_4O_7$ **FW:** 554.7 **Purity:** ≥98%
A solution in DMSO **Stability:** ≥1 year at -20°C
Summary: A potent anti-tumor agent used as a selective and irreversible inhibitor of the 20S proteasome; inhibits proteasome activity in cell growth assays (IC_{50} = 4 nM) and demonstrates potent cytotoxicity against B16-F10, HCT116, and Moser solid tumor cells, as well as P388 and K562 leukemia cells (IC_{50}s = 2-44 nM)

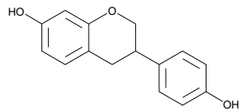
25 µg
50 µg
100 µg
250 µg



(±)-Equol 13184

[94105-90-5]
MF: $C_{15}H_{14}O_3$ **FW:** 242.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A nonsteroidal estrogen produced from the metabolism of the isoflavonoid phytoestrogen daidzein by human intestinal microflora; exhibits EC_{50} values of 200 and 74 nM for human ERα and ERβ, respectively; induces breast cancer cell proliferation *in vitro* at concentrations as low as 100 nM

5 mg
10 mg
25 mg
50 mg



(R)-Equol 10010172

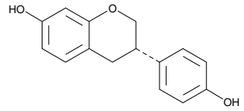
[221054-79-1] (+)-Equol, Isoequol
MF: $C_{15}H_{14}O_3$ **FW:** 242.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An ER agonist that binds to ERα and ERβ with K_i values of 27.4 and 15.4 nM, respectively; demonstrates higher ER agonist activity at ERα compared to ERβ (EC_{50} = 66 and 330 nM, respectively)

1 mg
5 mg
10 mg
25 mg

(S)-Equol 10010173

[531-95-3] 4′7-Dihydroxyisoflavan, (-)-Equol, 4′,7-Isoflavandiol
MF: $C_{15}H_{14}O_3$ **FW:** 242.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: The naturally occurring enantiomer of equol that demonstrates ER agonist activity similar to that of genistein (EC_{50} = 85 and 65 nM for human ERα and ERβ, respectively); preferentially binds ERβ (K_i = 0.73 nM) with lower affinity for ERα (K_i = 6.4 nM)

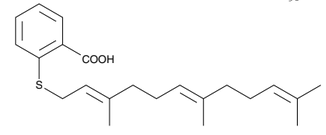
1 mg
5 mg
10 mg
25 mg



Farnesyl Thiosalicylic Acid 10010501

[162520-00-5] FTS, Salirasib
MF: $C_{22}H_{30}O_2S$ **FW:** 358.5 **Purity:** ≥96%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An inhibitor of Ras-mediated signaling that functions by dislodging Ras from the cell membrane thereby rendering it susceptible to proteolytic degradation; inhibits the growth of human Ha-ras-transformed Rat1 fibroblasts with an IC_{50} value of 7.5 µM

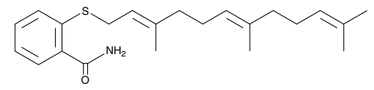
1 mg
5 mg
10 mg
25 mg



Farnesyl Thiosalicylic Acid Amide 13175

[1092521-74-8] FTS Amide, Salirasib Amide
MF: $C_{22}H_{31}NOS$ **FW:** 357.6 **Purity:** ≥96%
A solution in ethanol **Stability:** ≥1 year at -20°C
Summary: An inhibitor of Ras-mediated signaling that inhibits the growth of Panc-1 and U87 tumor cells with IC_{50} values of 20 and 10 µM, respectively

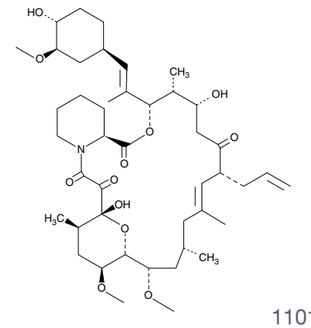
1 mg
5 mg
10 mg
50 mg



FK-506 10007965

[104987-11-3] Tacrolimus
MF: $C_{44}H_{69}NO_{12}$ **FW:** 804.0 **Purity:** ≥99%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent, clinically-useful immunosuppressant; binds to FK-506 binding protein 12 (K_i = 0.2 nM) to inhibit calcineurin; regulates NO neurotoxicity, neurotransmitter release, and regulation of Ca^{2+} release *via* the ryanodine and IP_3 receptors

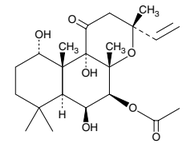
5 mg
10 mg
50 mg
100 mg



Forskolin 11018

[66575-29-9] Coleonol, HL 362, L 75-1362B, NSC 357088, NSC 375489
MF: $C_{22}H_{34}O_7$ **FW:** 410.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A naturally occurring diterpene that directly activates adenylyl cyclase to raise levels of cAMP in a wide variety of cell types; binds to type 1 adenylyl cyclase membranes with an IC_{50} value of 41 nM and demonstrates an EC_{50} value of 0.5 µM in an activation assay

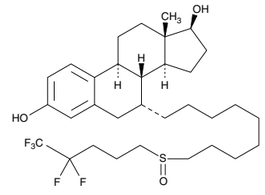
1 mg
5 mg
10 mg
50 mg



Fulvestrant 10011269

[129453-61-8] Faslodex®, ICI 182,780
MF: $C_{32}H_{47}F_5O_3S$ **FW:** 606.8 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent ER antagonist that works by both down-regulating and degrading ERα; efficacious in the treatment of estrogen-sensitive breast cancer; fully activates ER on hippocampal neurons

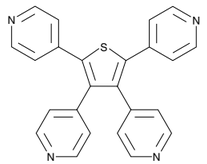
1 mg
5 mg
10 mg
50 mg



GANT 58 14193

[64048-12-0] NSC 75503
MF: $C_{24}H_{16}N_4S$ **FW:** 392.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: Inhibits GLI1-mediated transcription (EC_{50} = 5 µM) in a variety of cell types disrupting the hh signaling pathway downstream of Smo and Sufu; displays antiproliferative and antitumor activity against Ewing sarcoma family of tumor cells

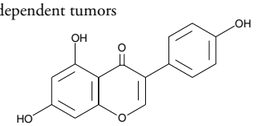
5 mg
10 mg
25 mg
50 mg



Genistein 10005167

[446-72-0]
MF: $C_{15}H_{10}O_5$ **FW:** 270.2 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An isoflavonoid phytoestrogenic compound found in soybeans, pea pods, and other legumes; acts as a tyrosine kinase inhibitor; has chemopreventive effects on breast, prostate, and other endocrine-dependent tumors

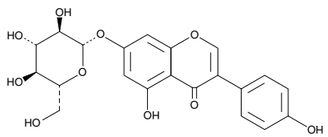
100 mg
250 mg
500 mg
1 g



Genistin 14174

[529-59-9] NSC 5112
MF: $C_{21}H_{20}O_{10}$ **FW:** 432.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A natural isoflavone which acts as a phytoestrogen; stimulates the growth of estrogen-dependent breast cancer cells *in vivo*; promotes the proliferation of bone marrow stromal cells and osteoblasts and suppresses bone turnover; increases bone formation in collagen matrix *in vivo*

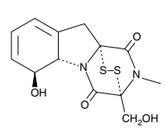
5 mg
10 mg
25 mg
50 mg



Gliotoxin 11433

[67-99-2] Aspergillin, S. N. 12870
MF: $C_{13}H_{14}N_2O_4S_2$ **FW:** 326.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An immunosuppressive mycotoxin which inhibits 20S proteasomal chymotrypsin activity (IC_{50} = 10 µM), preventing activation of NF-κB; induces apoptosis in monocytes and dendritic cells and reduces phagocytosis by neutrophils; inhibits geranylgeranyltransferase I and FTase (IC_{50} = 17 and 80 µM, respectively); potently suppresses viral infection by Nipah and Hendra virus *in vitro* (IC_{50} = 149 and 579 nM, respectively)

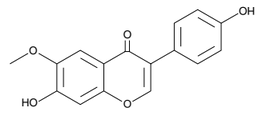
1 mg
5 mg
10 mg



Glycitein 14162

[40957-83-3]
MF: $C_{16}H_{12}O_5$ **FW:** 284.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An O-methylated isoflavone with weak estrogenic activity (IC_{50} = 3.94 µM) that has been used in research related phytoestrogen therapeutic activity applied to bone formation, cardiovascular disease, estrogen-dependent cancer, and Alzheimer's disease

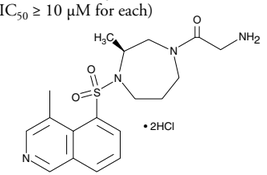
5 mg
10 mg
25 mg
50 mg



(S)-Glycyl-H-1152 (hydrochloride) 13332

[913844-45-8] Rho Kinase Inhibitor IV
MF: $C_{18}H_{24}N_4O_3S$ • 2HCl **FW:** 449.4 **Purity:** ≥98%
A solution in methanol **Stability:** ≥2 years at -20°C
Summary: A selective and potent Rho kinase inhibitor (IC_{50} = 11.8 nM for ROCK-II); poorly inhibits CaMKII, PKG, and Aurora A (IC_{50} = 2.57, 2.35, and 3.26 µM, respectively) as well as PKA or PKC (IC_{50} ≥ 10 µM for each)

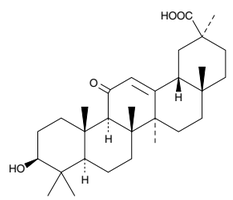
500 µg
1 mg
5 mg
10 mg



β-Glycyrrhetinic Acid 11845

[471-53-4] Arthrodont, Biosone, Enoxolone, GM 1658, NSC 35347, PO 12, STX 352
MF: $C_{30}H_{46}O_4$ **FW:** 470.7 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A major metabolite of glycyrrhizin, a constituent of licorice that exhibits anti-ulcerative, anti-inflammatory, and immunomodulatory properties; at 100 mg/kg/day, reduces lipid peroxidation and increases antioxidant activity in diabetic rats; suppresses LPS-induced TNF-α production and NF-κB activation in mouse macrophages 100-200 µM

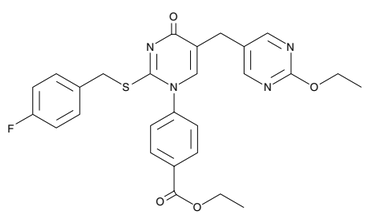
1 g
5 g
10 g



GW 1100 10008908

[306974-70-9]
MF: $C_{27}H_{25}FN_4O_4S$ **FW:** 520.6 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A selective antagonist of GPR40-mediated Ca^{2+} elevations in HEK293 cells (pIC_{50} = 5.99) without effecting those mediated by GPR120 at concentrations up to 10 µM; at 1 µM, inhibits the potentiating effects of GPR agonist, GW 9508 and linoleic acid on glucose-stimulated insulin secretion

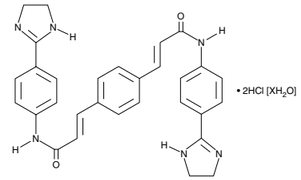
5 mg
10 mg
25 mg
50 mg



GW 4869 (hydrochloride hydrate) 13127

[6823-69-4]
MF: $C_{30}H_{28}N_6O_2$ • 2HCl [XH_2O] **FW:** 577.5 **Purity:** ≥90%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A cell-permeable, non-competitive inhibitor of neutral sphingomyelinases (IC_{50} = 1 µM), that does not affect acid sphingomyelinase activity; inhibits TNF-α-mediated sphingomyelin hydrolysis (100% inhibition at 20 µM) and TNF-α-induced cell death in MCF7 cells

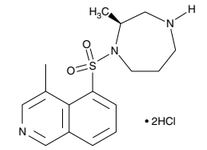
500 µg
1 mg
5 mg
10 mg



(S)-H-1152 (hydrochloride) 10007653

[451462-58-1]
MF: $C_{16}H_{21}N_3O_2S$ • 2HCl **FW:** 392.3 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent, specific, ATP-competitive, and cell permeable inhibitor of ROCK (K_i = 1.6 nM); more potent inhibitor of ROCK than either Y-27632 (K_i = 140 nM) or HA-1077 (K_i = 330 nM); poorly inhibits PKA, PKC, and MLCK

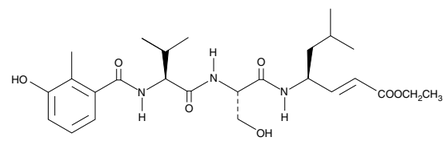
500 µg
1 mg
5 mg
10 mg



HMB-Val-Ser-Leu-VE 10007713

[862891-04-1]
MF: $C_{26}H_{39}N_3O_7$ **FW:** 505.6 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A tripeptide bearing a C-terminal vinyl ester which acts as a potent, selective inhibitor of the trypsin-like activity of the 20S proteasome (IC_{50} = 0.33 µM)

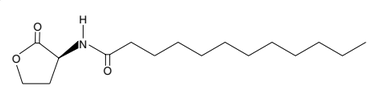
1 mg
5 mg
10 mg
25 mg



N-dodecanoyl-L-Homoserine lactone 10011203

[137173-46-7] C12-HSL, dDHL
MF: $C_{16}H_{29}NO_3$ **FW:** 283.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A small diffusible signaling molecule involved in quorum sensing, thereby controlling gene expression and affecting cellular metabolism in bacteria; activates NF-κB in RAW 264.7 macrophages, increasing the expression of TNF-α, IL-1β, and IL-8; alters cell cycling and metabolism of HaCaT cells

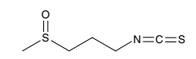
5 mg
10 mg
25 mg
50 mg



Iberin 14016

[505-44-2] NSC 321801
MF: $C_5H_9NOS_2$ **FW:** 163.3 **Purity:** ≥97%
A solution in ethanol **Stability:** ≥2 years at -20°C
Summary: A natural isothiocyanate which induces the expression of phase II detoxification enzymes and activates Nrf2, promoting the expression of antioxidant and phase II genes; acts as a quorum sensing inhibitor, blocking acyl-homoserine lactone signaling in *P. aeruginosa* without affecting growth (IC_{50} = 31-62 µM)

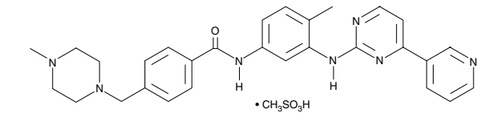
1 mg
5 mg
10 mg



Imatinib (mesylate) 13139

[220127-57-1] CGP57148B, Gleevec, Glivec, STI-571
MF: $C_{29}H_{31}N_7O$ • CH_4SO_3 **FW:** 589.7 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A first generation tyrosine kinase inhibitor that is used in the treatment of chronic myelogenous leukemia, gastrointestinal stromal tumor and other cancers; selectively targets certain tyrosine kinases, including c-ABL, PDGFR, KIT, and the oncoprotein BCR-ABL

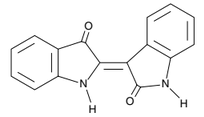
25 mg
50 mg
100 mg
500 mg



Indirubin 14155

[479-41-4] C.I. 73200, Couroupitine B, Indigopurpurin, NSC 105327
MF: $C_{16}H_{10}N_2O_2$ **FW:** 262.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A natural product with anti-inflammatory, anti-tumor, and neuroprotective effects; inhibits GSK-3 (IC_{50} = 2.5 µM) and CDK1 and 5 (IC_{50} = 10 µM for both isoforms)

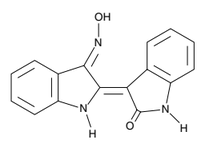
5 mg
10 mg
25 mg
50 mg



Indirubin-3'-monoxime 13314

[160807-49-8]
MF: $C_{16}H_{11}N_3O_2$ **FW:** 277.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent inhibitor of GSK-3β (IC_{50} = 22 nM), preventing tau phosphorylation both *in vitro* and *in vivo*

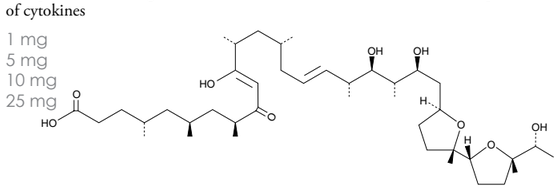
5 mg
10 mg
25 mg
50 mg



Ionomycin 10004974

[56092-81-0]
MF: $C_{41}H_{72}O_9$ **FW:** 709.0 **Purity:** ≥98%
A solution in ethanol **Stability:** ≥1 year at -20°C
Summary: A selective calcium ionophore that mobilizes intracellular calcium stores. It is used as a research tool to raise the intracellular level of calcium, to study calcium transport across biological membranes, and to stimulate the intracellular production of cytokines

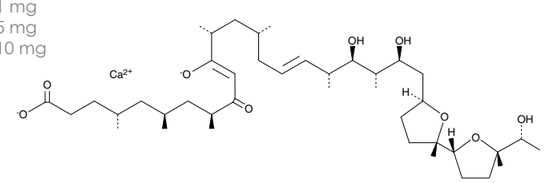
1 mg
5 mg
10 mg
25 mg



Ionomycin (calcium salt) 11932

[56092-82-1]
MF: $C_{41}H_{70}O_9$ • Ca **FW:** 747.1 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A selective calcium ionophore that mobilizes intracellular calcium stores. It is used as a research tool to raise the intracellular level of calcium, to study calcium transport across biological membranes, and to stimulate the intracellular production of cytokines

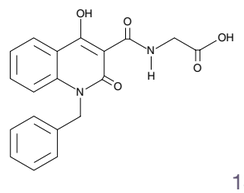
1 mg
5 mg
10 mg



IOX2 11573

[931398-72-0]
MF: $C_{19}H_{16}N_2O_5$ **FW:** 352.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: Potent, cell permeable inhibitor of PHD2 (IC_{50} value of 21 nM) with over 100-fold selectivity compared to inhibition of JMJD2A, JMJD2C, JMJD2E, JMJD3, or the 2OG oxygenase FIH (IC_{50}s <100 µM); inhibits HIF-1α hydroxylation in RCC4 cells at 50 µM

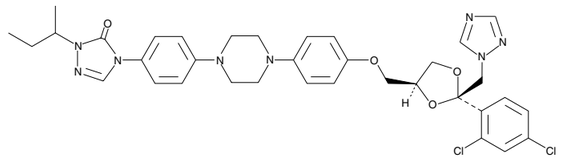
1 mg
5 mg
10 mg
50 mg



Itraconazole 13288

[84625-61-6]
MF: $C_{35}H_{38}Cl_2N_8O_4$ **FW:** 705.6 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An antifungal agent that acts as an inverse agonist to disrupt Hh signaling (IC_{50} = 0.8 µM); treatment at 100 mg/kg twice per day has been shown to suppress the growth of medulloblastomas from a *Ptch*$^{+/-}$*p53*$^{-/-}$ mouse allograft model

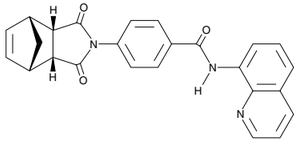
25 mg
50 mg
100 mg
250 mg



IWR-1-endo 13659

[1127442-82-3]
MF: $C_{25}H_{19}N_3O_3$ **FW:** 409.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent inhibitor of the Wnt response, blocking a cell-based Wnt/β-catenin pathway reporter response (IC_{50} = 180 nM); inhibits Wnt-induced accumulation of β-catenin, leading to proteasomal degradation of this protein

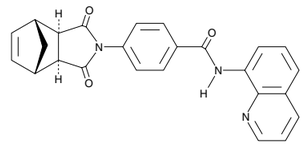
5 mg
10 mg
25 mg
50 mg



IWR-1-exo 13598

[1127442-87-8]
MF: $C_{25}H_{19}N_3O_3$ **FW:** 409.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An ideal control for the inhibitor of Wnt response compound, IWR-1-endo

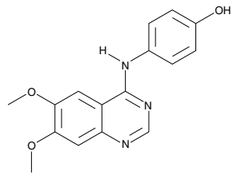
5 mg
10 mg
25 mg
50 mg



Janex 1 10011246

[202475-60-3] WHI-P131
MF: $C_{16}H_{15}N_5O_3$ **FW:** 297.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A selective inhibitor of JAK3 with an IC_{50} value of 78 µM that does not affect the enzymatic activity of JAK1, JAK2, or other protein tyrosine kinases (IC_{50} ≥ 350 µM); induces apoptosis in JAK3-expressing human leukemia cell lines NALM-6 and LC1;19 but not in melanoma or squamous carcinoma cell lines

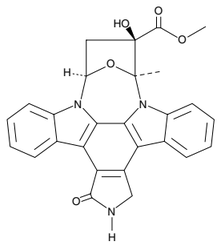
1 mg
5 mg
10 mg
25 mg



K252a 11338

[99533-80-9] SF 2370
MF: $C_{27}H_{21}N_3O_5$ **FW:** 467.5 **Purity:** ≥98%
A lyophilized powder **Stability:** ≥2 years at -20°C
Summary: A staurosporine analog that inhibits PKC, PKA, CaMKII, and phosphorylase kinase (IC_{50}s = 470, 140, 270, and 1.7 nM, respectively); inhibits PRK1 (IC_{50} = 3.2 nM *in vitro*), a PKC-related kinase that phosphorylates histone H3 at threonine 11

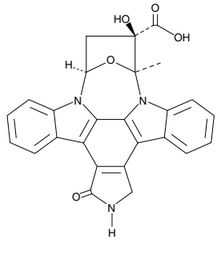
50 µg
100 µg
500 µg
1 mg



K252b 11339

[99570-78-2]
MF: $C_{26}H_{19}N_3O_5$ **FW:** 453.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A cell-impermeable kinase inhibitor, first described as an inhibitor of PKC; used to inhibit extracellular kinases (ectokinases) of cells in culture; inhibits receptor-mediated degranulation from RBL-2H3 cells (IC_{50} = 0.5 µg/ml); also used in comparison studies with the cell-permeable inhibitor K252a

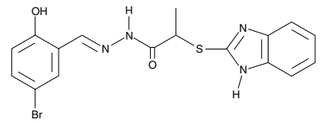
500 µg
1 mg



KH7 13243

[330676-02-3]
MF: $C_{17}H_{15}BrN_4O_2S$ **FW:** 419.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A selective inhibitor of soluble adenylyl cyclase with an IC_{50} value between 3-10 µM

5 mg
10 mg
25 mg
50 mg



Kinase Screening Library I (96-well) 10505

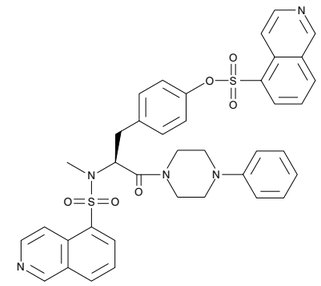
A 10 mM solution in DMSO **Stability:** ≥2 years at -20°C
Summary: The Kinase Screening Library contains specific and non-specific kinase inhibitors in a 96-well Matrix tube rack format as 10 mM stocks in DMSO. The library may include compounds such as PD 0325901 (dual specific threonine/tyrosine kinase inhibitor), U-0126 (selective MAP kinase inhibitor), SB 203580 (p38 MAPK inhibitor), and LY294002 (PI3K inhibitor). The composition of this screening library will always vary somewhat depending upon our inventory.

100 µl

KN-62 13318

[127191-97-3]
MF: $C_{38}H_{35}N_5O_6S_2$ **FW:** 721.9 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A selective, cell permeable inhibitor of CaMKII (IC_{50} = 900 nM)

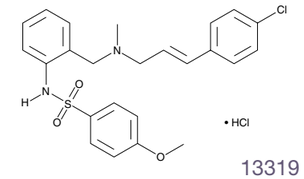
1 mg
5 mg
10 mg
25 mg



KN-92 (hydrochloride) 9000890

MF: $C_{24}H_{25}ClN_2O_3S$ • HCl **FW:** 493.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An inactive derivative of KN-93, the selective inhibitor of CaMKII; ineffective at inhibiting CaMKII or arresting cell growth of NIH 3T3 fibroblasts at concentrations up to 25 µM

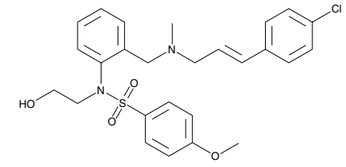
1 mg
5 mg
10 mg



KN-93 13319

[139298-40-1]
MF: $C_{26}H_{29}ClN_2O_4S$ **FW:** 501.0 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A selective inhibitor of CaMKII, competitively blocking CaM binding to the kinase (K_i = 370 nM); inhibits histamine-induced aminopyrine uptake in parietal cells (IC_{50} = 300 nM)

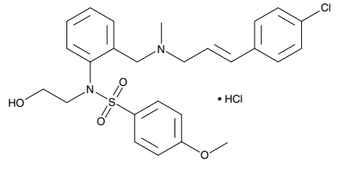
1 mg
5 mg
10 mg



KN-93 (hydrochloride) 13864

MF: $C_{26}H_{29}ClN_2O_4S$ • HCl **FW:** 537.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A selective inhibitor of CaMKII, competitively blocking CaM binding to the kinase (K_i = 370 nM); inhibits histamine-induced aminopyrine uptake in parietal cells (IC_{50} = 300 nM)

1 mg
5 mg
10 mg



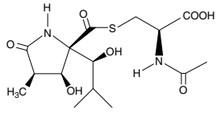
PKA, PKC, or PKG Inhibitors

Item No.	Product Name	Target	Effective Concentration
13298	Bisindolylmaleimide I	PKC	K_i = 14 nM
11020	Bisindolylmaleimide II	PDK1 PKA	IC_{50} = 14 µM IC_{50} = 2.94 µM
11072	Bisindolylmaleimide III	PKCα PDK1	IC_{50} = 3.8 µM
13299	Bisindolylmaleimide IV	PKC PKA	IC_{50}s range from 0.10-0.55 µM IC_{50}s range from 2-11.8 µM
13300	Bisindolylmaleimide V	PKC	IC_{50} >100 µM
13333	Bisindolylmaleimide VIII (acetate)	PKC	IC_{50} = 158 nM
13334	Bisindolylmaleimide IX (mesylate)	PKCα PKCβ1 PKCβ2 PKCγ PKCε	IC_{50} = 5 nM IC_{50} = 24 nM IC_{50} = 14 nM IC_{50} = 27 nM IC_{50} = 24 nM
11073	Bisindolylmaleimide XI (hydrochloride)	PKCα PKCβ1 PKCε	IC_{50} = 9 nM IC_{50} = 28 nM IC_{50} = 108 nM
11314	Chelerythrine chloride	PKC	IC_{50} = 660 nM
13311	Gö 6983	PKCα PKCβ PKCγ PKCδ PKCζ PKCµ	IC_{50} = 7 nM IC_{50} = 7 nM IC_{50} = 6 nM IC_{50} = 10 nM IC_{50} = 60 nM IC_{50} = 20,000 nM
10010249	H-8 (hydrochloride)	PKA PKG PKC	K_i = 1.2 µM K_i = 0.48 µM K_i = 15 µM
13312	H-9 (hydrochloride)	PKA PKC PKG	K_i = 1.9 µM K_i = 18 µM K_i = 0.87 µM
10010556	H-89	PKA	IC_{50} = 0.14 µM
11338	K252a	PKA PKC	IC_{50} = 140 nM IC_{50} = 470 nM
10011011	KT 5720	PKA	K_i = 60 nM
10010965	KT 5823	PKG	IC_{50} = 234 nM
13964	LY333531 (hydrochloride)	PKCβ1 PKCβ2	IC_{50} = 4.7 nM IC_{50} = 5.9 nM
10459	PKC 412	PKCα PKCβ PKCγ	IC_{50}s range from 80-500 nM
81590	Staurosporine	PKC	IC_{50} = 2.7 nM

Lactacystin 70980

[133343-34-7]
MF: $C_{15}H_{24}N_2O_7S$ **FW:** 376.4 **Purity:** ≥98%
A clear film **Stability:** ≥2 years at -20°C
Summary: A microbial metabolite isolated from *Streptomyces* that is widely used as a selective inhibitor of the 20S proteasome

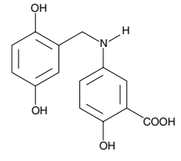
50 µg
100 µg
500 µg
1 mg



Lavendustin C 10010329

[125697-93-0] HDBA, NSC 666251
MF: $C_{14}H_{13}NO_5$ **FW:** 275.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent inhibitor of EGFR-associated tyrosine kinase with an IC_{50} value of 0.012 µM that also inhibits $pp60^{c\text{-}src(+)}$ kinase and CaMKII with IC_{50} values of 0.5 and 0.2 µM, respectively

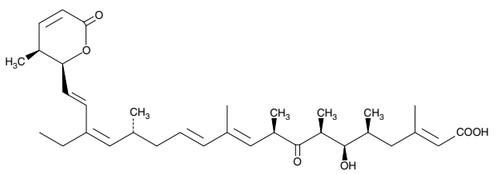
1 mg
5 mg
10 mg
50 mg



Leptomycin B 10004976

[87081-35-4] Elactocin, LMB, Mantuamycin, NSC 364372
MF: $C_{33}H_{48}O_6$ **FW:** 540.7 **Purity:** ≥98%
A solution in ethanol **Stability:** ≥1 year at -20°C
Summary: A potent anti-fungal antibiotic that can directly block nuclear transport by inhibiting the action of CRM1

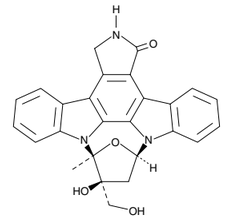
5 µg
10 µg
25 µg
50 µg



Lestaurtinib 12094

[111358-88-4] A 154475.0, CEP 701, KT 5555, SP 924
MF: $C_{25}H_{21}N_3O_4$ **FW:** 439.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A staurosporine analog that potently inhibits JAK2 kinase (IC_{50} = 1 nM) and downstream targets STAT5 (IC_{50} = 10-30 nM) and STAT3 in a human erythroleukemic cell line expressing the $JAK2^{V617F}$ mutation; potently inhibits the epigenetic kinase PRK1 (PKN1) *in vitro* (IC_{50} = 8.6 nM)

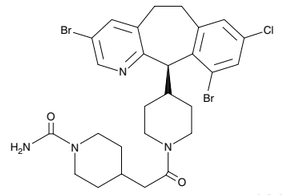
1 mg
5 mg
10 mg



Lonafarnib 11746

[193275-84-2] Sarasar, Sch 66336
MF: $C_{27}H_{31}Br_2ClN_4O_2$ **FW:** 638.8 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A farnesyl transferase inhibitor that blocks the post-translational lipid modification of oncogenic Ras isoforms H-Ras, N-Ras, and K-Ras (IC_{50}s = 1.9, 2.8, and 5.2 nM, respectively) and Ras homolog enriched in brain (IC_{50} = 10-100 nM); demonstrates potent dose-dependent oral activity in an array of human tumor xenograft models including tumors originating from colon, lung, pancreas, prostate, and urinary bladder

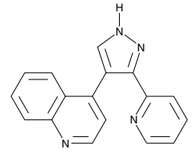
1 mg
5 mg
10 mg



LY364947 13341

[396129-53-6] HTS 466284, TGF-β R1 Kinase Inhibitor
MF: $C_{17}H_{12}N_4$ **FW:** 272.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A selective inhibitor of TGF-β RI, with an IC_{50} value of 59 nM; poorly inhibits TGF-β RII (IC_{50} = 400 nM), p38 MAPK (IC_{50} = 740 nM), and MLK-7 (IC_{50} = 1,400 nM); inhibits TGF-β-induced cell growth (IC_{50} = 89 nM) and Smad phosphorylation

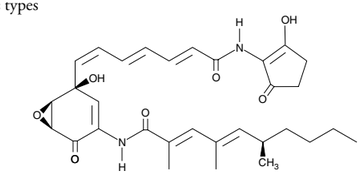
5 mg
10 mg
25 mg
50 mg



Manumycin A 10010497

[52665-74-4] NSC 622141, UCF 1C
MF: $C_{31}H_{38}N_2O_7$ **FW:** 550.7 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent and selective FTase inhibitor with anti-tumor activity: inhibits rat brain FTase with a K_i value of 1.2 µM, thereby preventing Ras activation; inhibits IKK in an number of cells types

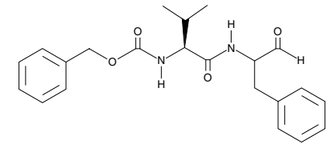
1 mg
5 mg



MDL 28170 14283

[88191-84-8] Calpain Inhibitor III
MF: $C_{22}H_{26}N_2O_4$ **FW:** 382.5 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A cell permeable, selective inhibitor of µ-calpain (calpain-1) and m-calpain (calpain-2); crosses the blood-brain barrier to inhibit brain cysteine protease activity; reported to have protective effects in numerous rodent models of neurotrauma and cardiac ischemia

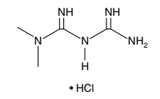
5 mg
10 mg
25 mg
50 mg



Metformin (hydrochloride) 13118

[1115-70-4] Apophage, Diaformin, Fornidd, Glucoformin, Glucophage, LA 6023, Melbin, Orabet, Riomet, Walaphage
MF: $C_4H_{11}N_5$ • HCl **FW:** 165.6 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A biguanide derivative used to lower blood glucose concentrations in patients with non-insulin-dependent diabetes mellitus; 50-400 mg/kg body weight inhibits complex 1 of the mitochondrial respiratory-chain and induces AMPK-dependent signaling in B6-Lep$^{ob/ob}$ mice

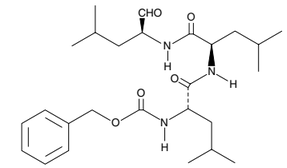
1 g
5 g

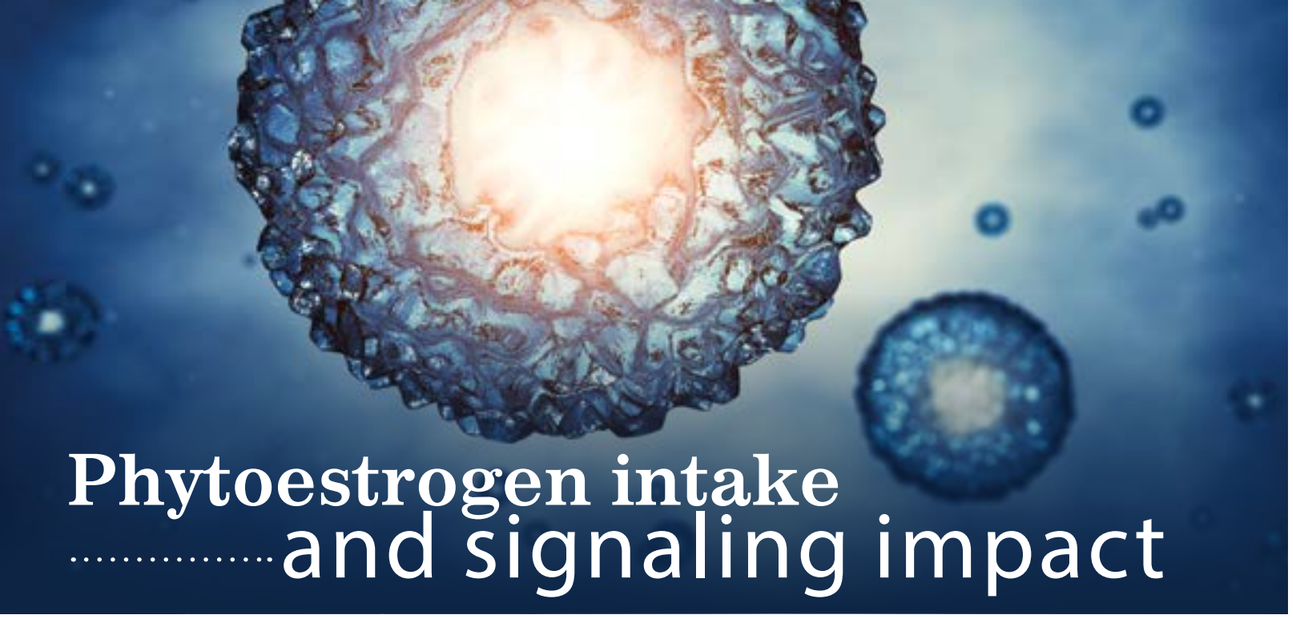


(R)-MG132 13697

[1211877-36-9]
MF: $C_{26}H_{41}N_3O_5$ **FW:** 475.6 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent, reversible and cell permeable proteasome inhibitor; a more effective inhibitor of chymotrypsin-like, trypsin-like, and peptidylglutamyl peptide hydrolyzing proteasome activities compared to (S)-MG132 (IC_{50}s = 0.22 *versus* 0.89 µM (ChTL); 34.4 *versus* 104.43 µM (TL); 2.95 *versus* 5.70 µM (PGPH), respectively)

1 mg
5 mg
10 mg
25 mg





Phytoestrogen intake and signaling impact

by [Olivia L. May, Ph.D.]

Phytoestrogens are non-steroidal, plant-derived compounds found in many different foods, most notably soy, that mimic the effects of estrogen. Recently, they've developed quite a double-edged reputation, for being either beneficial in lowering risk of osteoporosis, heart disease, breast cancer, and menopausal symptoms, or harmful as endocrine disruptors. The complexity of their effects seems to be tied to ethnicity, age, health status, level of consumption, and even the presence or absence of specific gut microflora. Historically, Asian populations, whose diet is traditionally soy-based, have lower rates of cardiovascular disease, menopausal symptoms, breast cancer (and other hormone-dependent cancers), diabetes, and obesity compared to Western populations. This observation has led to the widely held belief that consumption of soy foods reduces the risk of disease. Paradoxically, soy-derived phytoestrogens are known to act as weak estrogen agonists/antagonists that can behave similarly to synthetic endocrine disruptors (xenoestrogens) such as pesticides (DDT and methoxychlor), industrial lubricants (PCBs), and plasticizers (phthalates and Bisphenol A (BPA)). While the latter are frequently associated with disturbing statistics regarding declining reproductive health and increasing rates of cancer and obesity, phytoestrogens are still widely believed to be beneficial for their preventative or therapeutic actions in carcinogenesis, atherosclerosis, and osteoporosis.[1] Worldwide consumption of phytoestrogens has dramatically increased over the past few decades. They are present in numerous dietary supplements, infant formulas (up to ⅓ of US formulas contain soy), in many processed foods, and are widely marketed as a natural alternative to estrogen replacement therapy. This article examines the signaling pathways of phytoestrogens spanning from digestion to nuclear receptor activity, which may shed some light on the purported health benefits and adverse effects of soy consumption.

Phytoestrogen Consumption and Metabolism

Phytoestrogens are present as mixtures in foods, with isoflavones and lignans constituting a small portion of this class. Isoflavones occur naturally in the soybean as various forms of β-glucosides (*e.g.*, daidzin (Figure 1) and genistin), containing glucose or other carbohydrate moieties that are naturally biologically inert. They are bioactive only in the unconjugated (aglycone) form (*e.g.*, daidzein (Figure 1) and genistein). Thus, when consumed, isoflavone conjugates are not immediately absorbed into the systemic circulation. Upon reaching the intestine, conjugated isoflavones undergo deglycosylation by intestinal microbes and the actions of intestinal glucosidases.[2] Highly specific colon microflora, present in only 30-50% of the population (mostly vegetarians and individuals of Asian origin), are necessary to bioconvert daidzin to its metabolite daidzein, which is then further metabolized to equol (Figure 1) (and has an even greater estrogenic potency than daidzein).[3,4] It should be understood that the proportion of conjugated to unconjugated forms of isoflavones varies considerably among soy products. Generally, fermented soy foods, such as miso or tempeh, contain higher levels of aglycone than non-fermented soy-based foods. Interestingly, while the aglycones daidzein and genistein are the two most well-characterized isoflavones, most soy products have negligible amounts of these aglycones unless they have been added in supplement. Thus, interindividual differences in gut physiology as well as genetics and diet preferences together contribute to the bioavailability of phytoestrogens, which dictates their intracellular signaling potential.

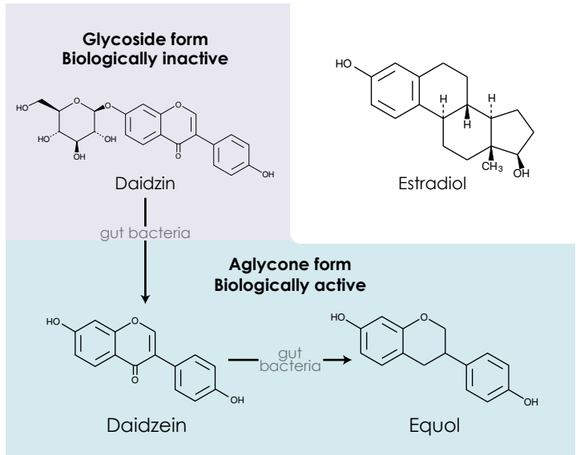


Figure 1. Metabolism of daidzin to the bioavailable equol.

Nuclear Receptor Signaling Initiated through Phytoestrogens

Isoflavones affect a wide array of intracellular signaling mechanisms important for regulating cellular growth and protection. They are known to inhibit the activity of protein tyrosine kinases leading to suppression of tumorigenesis. They down-regulate the expression of vascular endothelial growth factor (VEGF) and other related growth factor genes. Additionally, they can act as powerful antioxidant and anti-inflammatory agents. They also have a favorable role in numerous brain responses including synaptic plasticity and protection from neurodegeneration, as well as improving cardiovascular function. The most well-characterized mode of phytoestrogen action, however, is through estrogen receptor (ER) binding. Phytoestrogens can activate ER-dependent gene transcription by conformational binding to both ERα and ERβ, often demonstrating greater affinity toward ERβ than ERα (Table 1). ERα is expressed predominantly in endometrium, breast cancer cells, ovarian stroma cells, efferent duct epithelium, and the hypothalamus, whereas ERβ is expressed in kidney, brain, bone, heart, lungs, intestinal mucosa, prostate, and endothelial cells.[5,6] Thus, the preference of α- *versus* β- subtype binding is significant toward which phytoestrogens and other endocrine disruptors produce tissue-selective biological effects. Estrogen-like activity is typically desirable in bone, cardiovascular tissues, and the brain for functional maintenance, but has deleterious consequences if continually stimulated in breast and endometrial tissues. Once bound, isoflavones don't act as typical estrogen agonists, but rather more like selective estrogen receptor modulators (SERMS) with varying agonist/antagonist activities that are tissue specific and complexly dependent on the ratio of transcriptional co-activator and corepressor proteins present in each cell. Thus, the same ligand may be an agonist in certain tissues (where coactivators predominate) while acting as an antagonist in other tissues (where corepressors prevail). ER ligand binding induces unique conformational changes in the tertiary structure of the ER that influence the recruitment of these co-regulator proteins and interactions with the estrogen response element (ERE) present in the DNA of target genes. As one example, in the presence of genistein, ERβ is more efficient than ERα at recruiting the p160 coactivators TIF2 and SRC-1a, which potentiate transcriptional activity of ERs.[7] Generally, activation of ERβ has been shown to antagonize the growth promoting effect of ERα, which is mainly expressed in estrogen-sensitive tumor cells, thus producing a potential protective action against breast cancer incidence that is dependent on the ratio of active ERβ *versus* ERα.[5,8] Phytoestrogens bound to ERs can also activate transcription at AP-1 sites that bind Jun/Fos transcription factors.[9]

Non-nuclear Signaling of Phytoestrogens

Whereas ERs have classically been described as ligand-activated transcription factors (see Figure 2) mediating long-term genomic effects in hormonally-regulated tissues, estrogens and phytoestrogens can also mediate rapid, non-genomic actions that are typically associated with growth factor receptors and G protein–coupled receptors (GPCRs). In this case, ligand binding to specialized steroid membrane receptors triggers both rapid and transient activation of second messenger pathways, which are involved in regulating various cellular processes. GPR30, a member of the GPCR superfamily, is one such receptor that mediates estrogen-dependent kinase activation as well as transcriptional responses. GPR30 is the first identified transmembrane ER-bound GPCR that can bind several phytoestrogens, including genistein, and induce the activity of a truncated, 36-kDa variant of ERα, ERα36.[10-13] It has also been linked to the advancement of estrogen-related tumors through mitogen-activated protein kinase (MAPK) signaling pathways. GPR30 is predominantly expressed on the membrane of endoplasmic reticulum, so ligands must cross the plasma membrane to bind the receptor. When bound, heterotrimeric G proteins are activated (Figure 2), which then triggers either Src (which is involved in matrix metalloproteinases activation), adenylyl cyclase (which results in intracellular cAMP production), or phospholipase C (which produces inositol triphosphate (IP_3) and leads to intracellular calcium mobilization) (Figure 2). Matrix metalloproteinases cleave heparin-bound epidermal growth factor, freeing it to activate EGF receptors, leading to multiple downstream events, including activation of PI3K/Akt, and ERK/MAPK. Activation of Akt is closely related to survival, proliferation, and growth of cancer cells, and MAPK signaling initiates numerous cytosolic pathways, which further regulate transcription factors that often lead to tumor promotion.

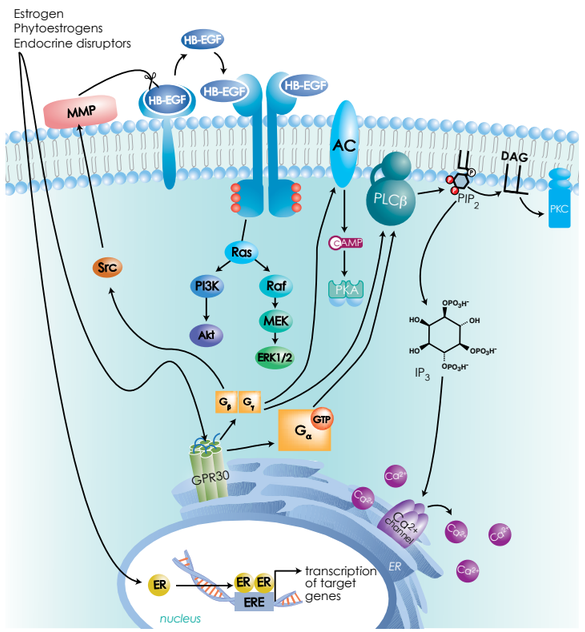


Figure 2. Intracellular signaling cascades initiated through both the classic nuclear estrogen receptor (ER) and the relatively novel GPR30 receptor.

Conclusion

While controversy ensues regarding their effectiveness and safety, indisputably the signaling capabilities and consequences of soy-derived estrogens are complicated. Cayman offers a curated selection of phytoestrogens (Table 1) to serve as helpful research tools to determine how this multitude of signaling capabilities can best be harnessed for therapeutic benefit. n

Table 1. Phytoestrogens available from Cayman

Item No.	Item Name	Summary of estrogenic activity
11730	Coumestrol	Binds ERα (IC_{50} = 11 nM) and ERβ (IC_{50} = 2 nM)
10005166	Daidzein	Binds both ERs with similar affinity (IC_{50}s = 4 μM)
13202	Daidzin	Anti-oxidant, anti-carcinogenic & anti-atherosclerotic activities
13109	Emodin	Binds ERα (K_i = 0.77 μM) and ERβ (K_i = 1.5 μM)
10112	(±)-Enterolactone	Reduces risk of acute coronary events & hormone-dependent cancers
13184	(±)-Equol	Binds ERα (EC_{50} = 200 nM) and ERβ (EC_{50} = 74 nM)
10010173	(S)-Equol	Binds ERβ (K_i = 0.73 nM) with lower affinity for ERα (K_i = 6.41 nM)
10010172	(R)-Equol *EXCLUSIVE*	Higher agonist activity at ERα (EC_{50} = 66 nM) than ERβ (EC_{50} = 330 nM)
10005167	Genistein	Binds with greater affinity to ERβ (IC_{50} = 0.2 μM) than ERα
14174	Genistin	Promotes proliferation of osteoblasts; suppresses bone turnover
14162	Glycitein	Weak binding of ERs (IC_{50}s = 3.9 μM)
14161	Glycitin	Promotes proliferation of osteoblasts; suppresses bone turnover
10005174	Matairesinol	Reduces incidence of breast cancer
14175	Puerarin	Antithrombotic, anti-allergic, and other salutary effects
10005169	Quercetin	Selectively binds ERβ over ERα
Estradiol (Item No. 10006315) is also available		

References

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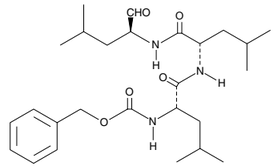
(S)-MG132 10012628

[133407-82-6] Z-Leu-Leu-Leu-CHO
MF: $C_{26}H_{41}N_3O_5$ **FW:** 475.6 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent, reversible, and cell permeable proteasome inhibitor; inhibits cell growth in B16 and IPC227F cells with IC_{50} values of 42 and 77 nM, respectively; inhibits NF-κB activation, sensitizing a variety of carcinoma cell lines to apoptosis

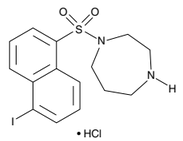
1 mg
5 mg
10 mg
50 mg



ML-7 (hydrochloride) 11801

[110448-33-4]
MF: $C_{15}H_{17}IN_2O_2S$ • HCl **FW:** 452.7 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: Inhibits smooth MLCK (K_i = 0.3 µM) 10-fold more potently than its parent compound ML-9

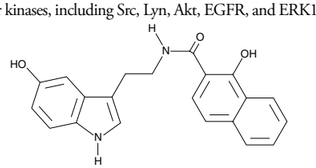
1 mg
5 mg
10 mg
50 mg



MS-1020 14273

[1255516-86-9]
MF: $C_{21}H_{18}N_2O_3$ **FW:** 346.4 **Purity:** ≥95%
A white to off-white solid **Stability:** ≥2 years at -20°C
Summary: A cell-permeable inhibitor of JAK3, strongly inhibiting constitutive autophosphorylation of JAK3 in L540 cells when used at 30-50 µM; without effect on other JAK isoforms and several other kinases, including Src, Lyn, Akt, EGFR, and ERK1/2

1 mg



MAPK Signaling Cascade Inhibitors

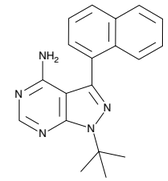
Item No.	Product Name	Target	Inhibitory Concentration
13297	AG-126	ERK1/ERK2	25-50 µM
11226	AS-703026	MEK1/2	
10009644	BAY-43-9006	Raf-1 B-Raf	IC_{50} = 6 nM IC_{50} = 22 nM
10010043	CAY10561	ERK2	K_i = 2 nM
10010400	CAY10571	p38 MAPK	
10460	Doramapimod	p38 MAPK	K_d = 0.1 µM
10010559	HA-1077 (hydrochloride)	ROCK-II PRK-2 MSK1 MAPKAP-K1b	IC_{50} = 1.9 µM IC_{50} = 4 µM IC_{50} = 5 µM IC_{50} = 15 µM
14399	MK 25 (hydrochloride)	MK2	IC_{50} = 0.11 µM
10010240	Olomoucine	ERK1/p44MAPK	IC_{50} = 25 µM
10006726	PD 98059	MAPKK1	IC_{50} = 2-7 µM
10006727	PD 169316	p38 MAPK	IC_{50} = 89 nM
10012431	PD 184161	MEK1/2	IC_{50} = 10-100 nM
13034	PD 0325901*	MEK	IC_{50} = 0.33 nM
10010399	SB 202190	p38α p38β	IC_{50} = 50 nM IC_{50} = 100 nM
13067	SB 203580	p38 MAPK	IC_{50} = 0.6 µM
13344	SB 203580 (hydrochloride)	p38 MAPK	IC_{50} = 0.6 µM
10009557	SC-1	RasGAP ERK1	K_d = 98 nM K_d = 212 nM
14156	SD 169	p38α p38β	IC_{50} = 3.2 nM IC_{50} = 122 nM
10009911	Tangeritin	ERK	IC_{50} ~3 µM
70970	U-0126	MEK1 MEK2	IC_{50} = 72 nM IC_{50} = 58 nM
13108	VX-702	p38α p38β	K_d = 3.7 nM K_d = 17 nM
10010367	ZM 336372	Raf-1	IC_{50} = 70 nM

**Sold for research purposes under agreement from Pfizer Inc.*

1-NA-PP1 10954

[221243-82-9] 1-Naphthyl-PP1, PP1 Analog
MF: $C_{19}H_{19}N_5$ **FW:** 317.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A reversible, cell-permeable inhibitor of Src-family tyrosine kinases that have been mutated, by a single base substitution, to become 'analog sensitive' (as), as compared to the wild-type kinase; inhibits v-Src-as1, with an I338G substitution, preferentially over v-Src (IC_{50} = 1.5 nM *versus* 1.0 µM, respectively); used to elucidate functions of several kinases in both mammalian and yeast systems

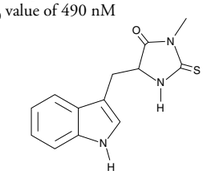
1 mg
5 mg
10 mg
50 mg



Necrostatin-1 11658

[4311-88-0] Nec-1
MF: $C_{13}H_{13}N_3OS$ **FW:** 259.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An inhibitor of RIP1 kinase that prevents the death of TNF-α-treated FADD-deficient Jurkat cells with an EC_{50} value of 490 nM

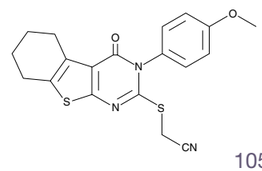
5 mg
10 mg
50 mg
100 mg



Necrostatin-5 10527

[337349-54-9] Nec-5
MF: $C_{19}H_{17}N_3O_2S_2$ **FW:** 383.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A selective allosteric inhibitor of RIP1 kinase that prevents the death of TNF-α-treated FADD-deficient Jurkat cells with an EC_{50} value of 240 nM

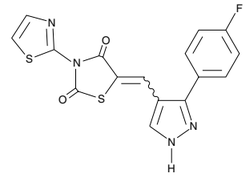
5 mg
25 mg



Necrostatin-7 10528

[351062-08-3] Nec-7
MF: $C_{16}H_{10}FN_5OS_2$ **FW:** 371.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: Inhibits TNF-α-induced necroptosis in a FADD-deficient variant of human Jurkat T cells with an EC_{50} value of 10.6 µM; structurally and biologically distinct from other necrostatins as it does not inhibit RIP1 kinase

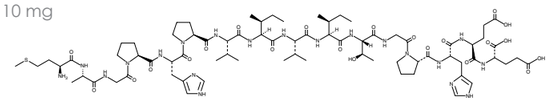
5 mg
25 mg



NFAT Inhibitor 13855

[249537-73-3] Nuclear Factor of Activated T cells
MF: $C_{75}H_{118}N_{20}O_{22}S$ **FW:** 1,683.9 **Purity:** ≥95%
A lyophilized powder **Stability:** ≥6 months at -20°C
Summary: A cell-permeable, selective inhibitor of calcineurin-mediated dephosphorylation of NFAT that does not disrupt other calcineurin-dependent pathways; disrupts NFAT-dependent expression of IL-2 and TNF-α when transfected in Jurak T cells and prevents the activation and proliferation of T cells both *in vitro* (~43% at 1 µM using mixed lymphocyte cultures) and *in vivo* (10 mg/kg using C3H/HeN mice)

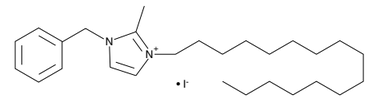
1 mg
5 mg
10 mg



NH125 10011250

[278603-08-0]
MF: $C_{27}H_{45}IN_2$ **FW:** 524.6 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An imidazole that has potent antibacterial properties in drug resistant bacteria; in bacteria, inhibits several histidine kinases, inhibiting YycG with an IC_{50} value of 6.6 µM; decreases the viability of several cancer cell lines with IC_{50} values ranging from 0.7-4.7 µM

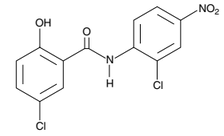
1 mg
5 mg
10 mg
50 mg



Niclosamide 10649

[50-65-7]
MF: $C_{13}H_8Cl_2N_2O_4$ **FW:** 327.1 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A salicylanilide compound with antihelminthic actions; specifically inhibits STAT3 (IC_{50} = 0.25 µM); inhibits the proliferation of Du145 prostate cancer cells, which have constitutively active STAT3 (IC_{50} = 0.7 µM)

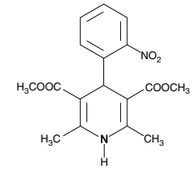
25 g
50 g
100 g
250 g



Nifedipine 11106

[21829-25-4] Adalat™, BAY 1040, Cordipin, Nifediac™, Nifedical™, Procardia™
MF: $C_{17}H_{18}N_2O_6$ **FW:** 346.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A dihydropyridine calcium channel blocker widely used as a coronary vasodilator for the treatment of hypertension and angina

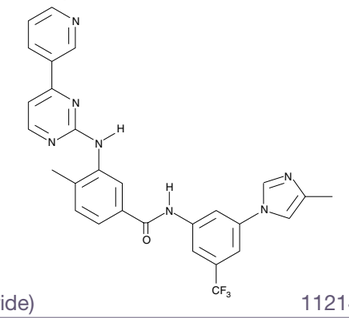
5 g
10 g
25 g



Nilotinib 10010422

[641571-10-0] AMN107
MF: $C_{28}H_{22}F_3N_7O$ **FW:** 529.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A tyrosine kinase inhibitor that potently inhibits Bcr/Abl tyrosine kinase and is effective in the treatment of certain leukemias; ~20-fold more potent than imatinib in inhibiting Bcr/Abl (*e.g.*, IC_{50} = 15 *versus* 280 nM, respectively)

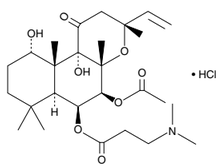
5 mg
10 mg
25 mg
50 mg



NKH477 (hydrochloride) 11214

[138605-00-2] Adehl, Colforsin Dapropate
MF: $C_{27}H_{43}NO_8$ • HCl **FW:** 546.1 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A water-soluble analog of forskolin which has both inotropic and vasodilator effects when administered intravenously; stimulates cardiac (type V) adenylyl cyclase more potently than other isoforms; relaxes guinea pig tracheal smooth muscle precontracted with histamine with an EC_{50} value of 32.6 nM

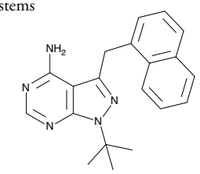
1 mg
5 mg
10 mg



1-NM-PP1 13330

[221244-14-0] PP1 Analog II
MF: $C_{20}H_{21}N_5$ **FW:** 331.4 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A cell permeable inhibitor of kinases that have been mutated, by a single base substitution, to become 'analog sensitive' (as), as compared to the wild-type kinase; inhibits v-Src-as1, with an I338G substitution, preferentially over v-Src (IC_{50} = 4.2 nM *versus* 28 µM, respectively); used to elucidate functions of several kinases in both mammalian and yeast systems

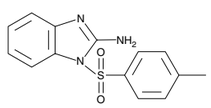
1 mg
5 mg
10 mg
25 mg



Nodinitib-1 11040

[799264-47-4] CID-1088438, ML130
MF: $C_{14}H_{13}N_3O_2S$ **FW:** 287.3 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: Selectively inhibits NOD1-dependent activation of NF-κB and MAPK signaling (IC_{50} = 0.6 µM) and also inhibits NOD1-induced IL-8 production in MCF-7 cells without affecting viability

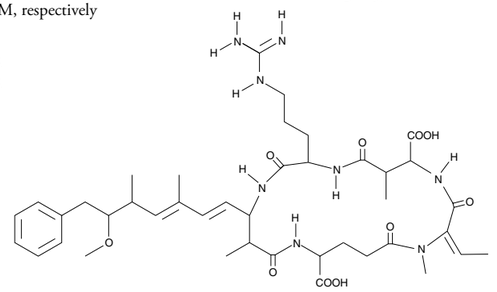
5 mg
10 mg
25 mg
50 mg



Nodularin 10007190

[118399-22-7]
MF: $C_{41}H_{60}N_8O_{10}$ **FW:** 825.0 **Purity:** ≥95%
A solution in ethanol **Stability:** ≥1 year at -20°C
Summary: A hepatotoxic monocylic pentapeptide that acts as a potent inhibitor of protein phosphatase types 1 (PP1) and 2A (PP2A), exhibiting IC_{50} values of 1.8 and 0.026 nM, respectively

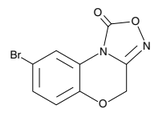
50 µg
100 µg
500 µg
1 mg



NS-2028 81600

[204326-43-2]
MF: $C_9H_5BrN_2O_3$ **FW:** 269.1 **Purity:** ≥99%
A crystalline solid **Stability:** ≥1 year at -20°C
Summary: A specific irreversible inhibitor of soluble guanylyl cyclase; inhibits purified bovine lung guanylyl cyclase with IC_{50} values of 30 and 200 nM for basal and NO-stimulated enzymes, respectively

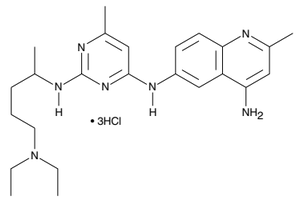
1 mg
5 mg
10 mg
25 mg



NSC 23766 (hydrochloride) 13196

[1177865-17-6]
MF: $C_{24}H_{35}N_7$ • 3HCl **FW:** 531.0 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A cell-permeable, reversible inhibitor of Rac1 activation by the Rac1-specific GEFs TrioN and Tiam 1 (IC_{50} = 50 µM); has no effect on the closely related GTPases, Cdc42, and RhoA

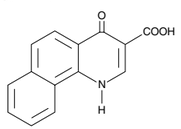
1 mg
5 mg
10 mg
25 mg



NSC 210902 10011255

[51726-83-1]
MF: $C_{14}H_9NO_3$ **FW:** 239.2 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A selective CK2 inhibitor (IC_{50} = 1 µM) that inhibits binding of ATP with a K_i value of 0.28 µM

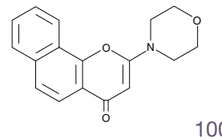
1 mg
5 mg
10 mg
50 mg



NU 7026 13308

[154447-35-5] DNA-PK Inhibitor II, LY293646
MF: $C_{17}H_{15}NO_3$ **FW:** 281.3 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A cell-permeable, potent, specific, and ATP-competitive inhibitor of DNA-PK (IC_{50} = 230 nM); poorly inhibits PI3K (IC_{50} = 13 µM) and is inactive against ATM, ATR, and PARP-1

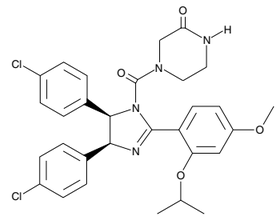
5 mg
10 mg
25 mg
50 mg



(±)-Nutlin-3 10004372

[548472-68-0]
MF: $C_{30}H_{30}Cl_2N_4O_4$ **FW:** 581.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥1 year at -20°C
Summary: An inhibitor of p53-Mdm2 interaction (IC_{50} = 0.09 µM); induces the expression of p53-regulated genes and exhibits potent antiproliferative activity in cells with functional p53

1 mg
5 mg
10 mg
50 mg

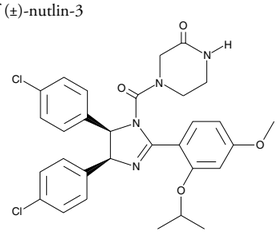


NOTE: Sold under license from Hoffman-La Roche

(+)-Nutlin-3 10009816

Nutlin 3b
MF: $C_{30}H_{30}Cl_2N_4O_4$ **FW:** 581.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An inactive enantiomer of nutlin-3 that may serve as a useful control for non-Mdm2 related cellular activities; also called enantiomer b based on the elution pattern during chiral separation of (±)-nutlin-3

1 mg
5 mg
10 mg
25 mg

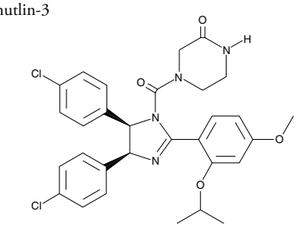


NOTE: Sold under license from Hoffman-La Roche

(-)-Nutlin-3 18585

Nutlin 3a
MF: $C_{30}H_{30}Cl_2N_4O_4$ **FW:** 581.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent inhibitor of Mdm2-p53 binding (IC_{50} = 0.09 µM); induces the expression of p53-regulated genes and exhibits potent antiproliferative activity in cells with functional p53; also called enantiomer a based on the elution pattern during chiral separation of (±)-nutlin-3

1 mg
5 mg
10 mg
25 mg

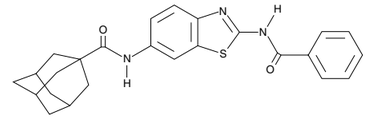


NOTE: Sold under license from Hoffman-La Roche

NVP-231 13858

[362003-83-6]
MF: $C_{25}H_{25}N_3O_2S$ **FW:** 431.6 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent, reversible inhibitor of ceramide kinase (IC_{50} = 12 nM), which has minimal effect on several other lipid kinases, including sphingosine kinases 1 and 2

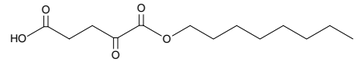
1 mg
5 mg
10 mg



Octyl-α-ketoglutarate 11970

[876150-14-0] α-KG octyl ester
MF: $C_{13}H_{22}O_5$ **FW:** 258.3 **Purity:** ≥95%
A solution in methyl acetate **Stability:** ≥1 year at -20°C
Summary: A stable, cell-permeable form of α-ketoglutarate which accumulates rapidly and preferentially in cells with a dysfunctional tricarboxylic acid cycle; stimulates PHD activity and increases HIF-1α turnover when used at 1 mM; competitively blocks succinate- or fumarate-mediated inhibition of PHD

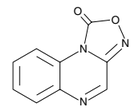
1 mg
5 mg
10 mg



ODQ 81410

[41443-28-1]
MF: $C_9H_5N_3O_2$ **FW:** 187.2 **Purity:** ≥98%
A crystalline solid **Stability:** ≥1 year at -20°C
Summary: A highly selective, irreversible, heme-site inhibitor of soluble guanylyl cyclase

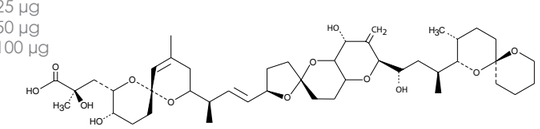
5 mg
10 mg
50 mg
100 mg



Okadaic Acid 10011490

[78111-17-8] Acanthifolicin, 35-Demethyl-DTX 1, NSC 677083
MF: $C_{44}H_{68}O_{13}$ **FW:** 805.0 **Purity:** ≥95%
A solution in ethanol **Stability:** ≥2 years at -20°C
Summary: A potent inhibitor of certain serine/threonine protein phosphatases, targeting the multiple isoforms of PP1 (IC_{50} = 10-50 nM), both isoforms of PP2A (IC_{50} = 0.5 nM) and PP3 (IC_{50} = 4 nM); a very weak inhibitor of PP2B (IC_{50} > 2 µM); does not inhibit PP2C or other phosphatases

25 µg
50 µg
100 µg



PPAR Antagonists

Item No.	Product Name	Target	Effective Concentration
70790	BADGE	PPARγ	K_d = 100 µM
70785	GW 9662	PPARγ	≥90% effective at 0.1 µM
10010324	Harmine	PPARγ	*via* inhibition of Wnt
10026	T0070907	PPARγ	IC_{50} = 1 nM

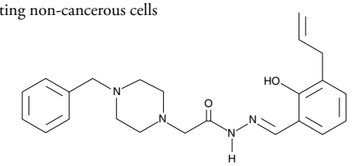
PPAR Agonists

Item No.	Product Name	Target	Effective Concentration
13452	AM3102	PPARα	EC_{50} = 100 nM
10009145	Bezafibrate	PPARα PPARδ PPARγ	EC_{50} = 50 µM EC_{50} = 20 µM EC_{50} = 60 µM
9000183	Carbaprostacyclin methyl ester	PPARδ	
10009079	CAY10506	PPARγ	EC_{50} = 10 µM
10009017	CAY10514	PPARα PPARγ	EC_{50} = 0.17 µM EC_{50} = 0.64 µM
10008846	CAY10573	PPARα PPARδ PPARγ	IC_{50} = 113 nM IC_{50} = 50 nM IC_{50} = 223 nM
10012536	CAY10592	PPARδ	EC_{50} = 53 nM (transactivation assays) EC_{50} = 30 nM (oxidation of free fatty acid)
13282	CAY10599	PPARγ PPARα PPARδ	EC_{50} = 0.05 µM EC_{50} = 3.99 µM EC_{50} > 10 µM
71730	Ciglitazone	PPARγ	EC_{50} = 3.0 µM
10956	Clofibrate	PPARα	EC_{50} = 50 nM (mouse) EC_{50} = 55 nM (human)
9000347	17-keto-7(Z),10(Z),13(Z),15(E),19(Z)-Docosapentaenoic Acid	PPARγ	EC_{50} = ~200 µM
10005368	Fenofibrate	PPARα	EC_{50} = 18 nM (mouse) EC_{50} = 30 nM (human)
10004888	FMOC-L-Leucine	PPARγ	K_i = 15 µM
11908	GQ-16	PPARγ	K_i = 160 nM
10006798	GW 0742	PPARδ	EC_{50} = 1.1 nM
10008613	GW 7647	PPARα PPARγ PPARδ	EC_{50} = 0.006 µM EC_{50} = 1.1 µM EC_{50} = 6.2 µM
10011211	GW 9578	PPARα	EC_{50} = 0.005 µM (mouse) EC_{50} = 0.05 µM (human)
10009880	GW 590735	PPARα	EC_{50} = 4 nM
10009661	N-Octadecyl-N'-propyl-sulfamide	PPARα	EC_{50} = 100 nM
71000	PPARγ Ligand Pack	Contains the PPARγ ligands Ciglitazone, Rosiglitazone, Troglitazone, and 15-deoxy-$\Delta^{12,14}$-Prostaglandin J_2. Also contains the selective PPARγ antagonist GW 9662.	
71740	Rosiglitazone	PPARγ	K_d = 43 nM
11884	Rosiglitazone Maleate	PPARγ	K_d = 43 nM
71742	Rosiglitazone (potassium salt)	PPARγ	K_d = 43 nM
11615	Telmisartan	PPARγ	EC_{50} = 4.5 µM
90500	3-Thiatetradecanoic Acid	PPAR	
71750	Troglitazone	PPARγ	EC_{50} = 0.55 µM (human) EC_{50} = 0.78 µM (mouse)
70730	Wy 14643	PPARα PPARγ	

PAC-1 10009317

[315183-21-2] Procaspase-activating Compound 1
MF: $C_{23}H_{28}N_4O_2$ **FW:** 392.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A procaspase-3 activator and a potential drug treatment in cancer cell lines with elevated levels of procaspase-3; exhibits an IC_{50} value of 3 nM for induction of cancer cell death without affecting non-cancerous cells

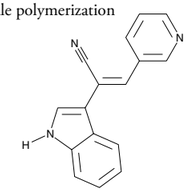
25 mg
50 mg
100 mg
250 mg



Paprotrain 10524

[57046-73-8] Passenger Proteins Transport Inhibitor
MF: $C_{16}H_{11}N_3$ **FW:** 245.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A selective, cell-permeable, reversible inhibitor of mitotic kinesin-like protein-2 (IC_{50}s = 0.83-1.35 µM); treatment with 10-50 µM results in binucleated cells, perturbing relocation of Aurora B kinase and survivin to the central spindle in anaphase cells without affecting microtubule polymerization

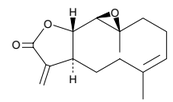
1 mg



Parthenolide 70080

[20554-84-1]
MF: $C_{15}H_{20}O_3$ **FW:** 248.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A natural sesquiterpene lactone which inhibits the growth of the promastigote form of *L. amazonensis* (IC_{50} = 3.6 µg/ml); induces apoptosis in cancer cells, at least in part by inhibiting NF-κB- and STAT-mediated anti-apoptotic gene transcription; directly binds the pattern recognition receptor NOD2

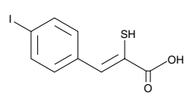
25 mg
50 mg
100 mg



PD 150606 13859

[179528-45-1]
MF: $C_9H_7IO_2S$ **FW:** 306.1 **Purity:** ≥98%
An off-white solid **Stability:** ≥2 years at -20°C
Summary: A selective, cell-permeable inhibitor of calpains (K_i = 0.21 µM for µ-calpain (calpain-1) and 0.37 µM for m-calpain (calpain-2))

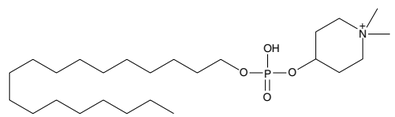
5 mg
25 mg



Perifosine 10008112

[157716-52-4]
MF: $C_{25}H_{53}NO_4P$ **FW:** 462.7 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An alkylphospholipid that induces apoptotic cell death in a time- and dose-dependent manner in a variety of tumor cell lines but not in normal vascular endothelial cells; causes inhibition of PC-3 prostate carcinoma cell growth (GI_{50} = 5 µM at 24h) associated with rapidly decreased Akt activation; induces p21WAF1 expression in squamous carcinoma cells, leading to loss in CDK activity and cell cycle arrest

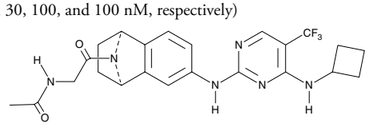
1 mg
5 mg
10 mg
50 mg



PF-03814735 15015

[942487-16-3]
MF: $C_{23}H_{25}F_3N_6O_2$ **FW:** 474.5 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A reversible inhibitor of both Aurora A and B kinases (IC_{50}s = 0.8 and 5 nM, respectively); also inhibits Flt1, FAK, TrkA, Met, and fibroblast growth factor receptor 1 (IC_{50}s = 10, 22, 30, 100, and 100 nM, respectively)

1 mg
5 mg
10 mg
50 mg

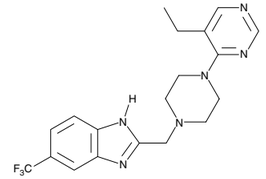


NOTE: Sold for research purposes under agreement from Pfizer Inc.

PF-04708671 15018

[1255517-76-0]
MF: $C_{19}H_{21}F_3N_6$ **FW:** 390.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A specific, cell-permeable inhibitor of S6K1 (IC_{50} = 160 nM); does not inhibit S6K2, MSK, or RSK, or many other unrelated kinases, under conditions in which it inhibits S6K1 activity

10 mg
25 mg
50 mg
100 mg

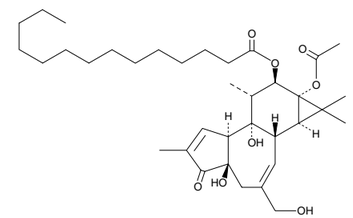


NOTE: Sold for research purposes under agreement from Pfizer Inc.

Phorbol 12-myristate 13-acetate 10008014

[16561-29-8] PMA, 12-O-Tetradecanoylphorbol-13-acetate, TPA
MF: $C_{36}H_{56}O_8$ **FW:** 616.8 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A phorbol ester that is commonly used to activate certain types of PKC and, indirectly, certain MAP kinase pathways; prolonged treatment with PMA produces various effects, ranging from tumorigenesis to hematopoietic differentiation

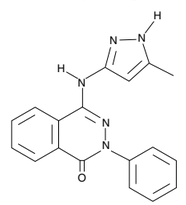
1 mg
5 mg
10 mg
25 mg



Phthalazinone pyrazole 10735

[880487-62-7]
MF: $C_{18}H_{15}N_5O$ **FW:** 317.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent inhibitor of Aurora A kinase (IC_{50} = 31 nM); does not inhibit Aurora B kinase at doses up to 100 µM; inhibits the proliferation of HCT116, Colo205, and MCF-7 cells (IC_{50} = 7.8, 2.9, and 1.6 µM, respectively)

1 mg
5 mg
10 mg



Inositol Phospholipids

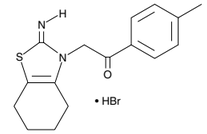
Item No.	Product Name
10008439	D-*myo*-Inositol-1,2-diphosphate (sodium salt)
10008443	D-*myo*-Inositol-1,3-diphosphate (sodium salt)
10008438	D-*myo*-Inositol-1,4-diphosphate (sodium salt)
10008441	D-*myo*-Inositol-1,5-diphosphate (sodium salt)
10008419	D-*myo*-Inositol-2,4-diphosphate (sodium salt)
10008418	D-*myo*-Inositol-4,5-diphosphate (sodium salt)
10008453	D-*myo*-Inositol-1,2,3,5,6-pentaphosphate (sodium salt)
10008452	D-*myo*-Inositol-1,2,4,5,6-pentaphosphate (sodium salt)
10009851	D-*myo*-Inositol-1,3,4,5,6-pentaphosphate (ammonium salt)
10007784	D-*myo*-Inositol-1,3,4,5,6-pentaphosphate (sodium salt)
9001248	D-*myo*-Inositol-1-phosphate (cyclohexyl ammonium salt)
10007777	D-*myo*-Inositol-1-phosphate (sodium salt)
10007778	D-*myo*-Inositol-3-phosphate (sodium salt)
10008437	D-*myo*-Inositol-4-phosphate (ammonium salt)
10008448	D-*myo*-Inositol-1,2,3,4-tetraphosphate (sodium salt)
10008449	D-*myo*-Inositol-1,2,3,5-tetraphosphate (sodium salt)
10008450	D-*myo*-Inositol-1,2,3,6-tetraphosphate (sodium salt)
10008451	D-*myo*-Inositol-1,2,4,5-tetraphosphate (sodium salt)
10008444	D-*myo*-Inositol-1,2,5,6-tetraphosphate (sodium salt)
60980	D-*myo*-Inositol-1,3,4,5-tetraphosphate (sodium salt)
10008442	D-*myo*-Inositol-1,3,4,6-tetraphosphate (ammonium salt)
10007783	D-*myo*-Inositol-1,4,5,6-tetraphosphate (sodium salt)
10008456	D-*myo*-Inositol-2,3,4,5-tetraphosphate (ammonium salt)
10008455	D-*myo*-Inositol-2,3,5,6-tetraphosphate (sodium salt)
10007782	D-*myo*-Inositol-3,4,5,6-tetraphosphate (sodium salt)
10007780	D-*myo*-Inositol-1,2,6-triphosphate (sodium salt)
60972	D-*myo*-Inositol-1,3,4-triphosphate (sodium salt)
10007781	D-*myo*-Inositol-1,3,5-triphosphate (sodium salt)
60960	D-*myo*-Inositol-1,4,5-triphosphate (potassium salt)
10008205	D-*myo*-Inositol-1,4,5-triphosphate (sodium salt)
10008426	L-*myo*-Inositol-1,4,5-triphosphate (sodium salt)
10008427	D-*myo*-Inositol-1,4,6-triphosphate (sodium salt)
10008422	D-*myo*-Inositol-1,5,6-triphosphate (sodium salt)
10008423	D-*myo*-Inositol-2,3,5-triphosphate (ammonium salt)
10007779	D-*myo*-Inositol-2,4,5-triphosphate (sodium salt)
10008424	D-*myo*-Inositol-2,5,6-triphosphate (sodium salt)
10008425	D-*myo*-Inositol-3,4,5-triphosphate (sodium salt)

Item No.	Product Name
10007839	PLC thio-PIP_2 (sodium salt)
9000304	PtdIns-(1-arachidonoyl-d_8, 2-arachidonoyl) (sodium salt)
9000305	PtdIns-(1-arachidonoyl, 2-arachidonoyl-d_8) (ammonium salt)
9000660	PtdIns-(1,2-dihexanoyl) (sodium salt)
10008099	PtdIns-(1,2-dioctanoyl) (sodium salt)
10007710	PtdIns-(1,2-dipalmitoyl) (ammonium salt)
10007759	PtdIns-(3,4)-P_2 (1,2-dihexanoyl) (sodium salt)
10008390	PtdIns-(3,4,5)-P_3 (1,2-dihexanoyl) (ammonium salt)
9000829	PtdIns-(3,4,5)-P_3 (1-stearoyl, 2-docosahexaenoyl) (sodium salt)
10008396	PtdIns-(3,5)-P_2 (1,2-dihexanoyl) (sodium salt)
9000656	PtdIns-(4)-P_1 (1,2-dioctanoyl)-biotin (sodium salt)
10007757	PtdIns-(4)-P_1 (1,2-dihexanoyl) (sodium salt)
10007762	PtdIns-(4,5)-P_2 (1,2-dihexanoyl) (sodium salt)
10008050	PtdIns-(5)-P_1 (1,2-dihexanoyl) (sodium salt)
10008394	PtdIns-(3)-P_1 (1,2-dioctanoyl) (sodium salt)
10008400	PtdIns-(3,4)-P_2 (1,2-dioctanoyl) (sodium salt)
10010181	Ptd(S)Ins-(3,4)-P_2 (1,2-dioctanoyl) (sodium salt)
10007764	PtdIns-(3,4,5)-P_3 (1,2-dioctanoyl) (sodium salt)
10009804	3-PT-PtdIns-(3,4,5)-P_3 (1,2-dioctanoyl) (sodium salt)
10009531	PtdIns-(3,4,5)-P_3-biotin (sodium salt)
10010383	PtdIns-(3,4,5)-P_3-fluorescein (ammonium salt)
10008398	PtdIns-(3,5)-P_2 (1,2-dipalmitoyl) (sodium salt)
10007763	PtdIns-(3,5)-P_2 (1,2-dioctanoyl) (sodium salt)
10007711	PtdIns-(4)-P_1 (1,2-dioctanoyl) (ammonium salt)
64910	PtdIns-(4,5)-P_2 (1,2-dioctanoyl) (sodium salt)
10008159	PtdIns-(4,5)-P_2-biotin (sodium salt)
10010388	PtdIns-(4,5)-P_2-fluorescein (ammonium salt)
10007758	PtdIns-(5)-P_1 (1,2-dioctanoyl) (ammonium salt)
64921	PtdIns-(3)-P_1 (1,2-dipalmitoyl) (ammonium salt)
10005616	PtdIns-(3)-P_1 (1,2-dipalmitoyl)-d_{62} (ammonium salt)
64922	PtdIns-(3,4)-P_2 (1,2-dipalmitoyl) (sodium salt)
10010112	Ptd(S)Ins-(3,4)-P_2 (1,2-dipalmitoyl) (sodium salt)
64920	PtdIns-(3,4,5)-P_3 (1,2-dipalmitoyl) (sodium salt)
9000414	PtdIns-(3,4,5)-P_3 (1,2-dipalmitoyl)-d_{62} (sodium salt)
64923	PtdIns-(4)-P_1 (1,2-dipalmitoyl) (ammonium salt)
9000655	PtdIns (4)-P_1-fluorescein (ammonium salt)
64924	PtdIns-(4,5)-P_2 (1,2-dipalmitoyl) (ammonium salt)
10008115	PtdIns-(4,5)-P_2 (1,2-dipalmitoyl) (sodium salt)
10005615	PtdIns-(4,5)-P_2 (1,2-dipamitoyl)-d_{62} (sodium salt)
64925	PtdIns-(5)-P_1 (1,2-dipalmitoyl) (ammonium salt)
64930	PtdIns-(3,4,5)-P_3 (1-stearoyl, 2-arachidonoyl) (sodium salt)

Pifithrin-α 13326

[63208-82-2] PFT-α
MF: $C_{16}H_{18}N_2OS$ • HBr **FW:** 367.3 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An inactivator of p53 that blocks p53-dependent transcriptional activation and apoptosis, preventing p53-mediated apoptosis by cytotoxic compounds in C8 cells at 10 µM and in human umbilical vein endothelial cells at 30 µM

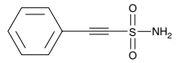
5 mg
10 mg
25 mg
50 mg



Pifithrin-μ 10748

[64984-31-2] PFT-μ, 2-Phenylethynesulfonamide
MF: $C_8H_7NO_2S$ **FW:** 181.2 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An inhibitor of p53-mediated apoptosis, preventing p53 binding at the mitochondrial surface without affecting p53 transactivational activities; at 25 µM, pifithrin-μ reduces p53-mediated apoptosis triggered by nutlin; also interacts selectively with HSP70, disrupting its association with many substrate proteins

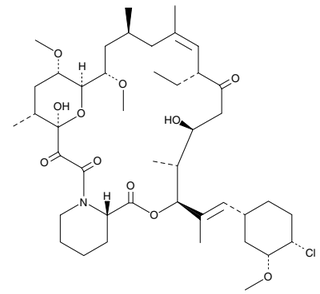
5 mg
10 mg
25 mg
50 mg



Pimecrolimus 13107

[137071-32-0] Elidel, SDZ-ASM 981
MF: $C_{43}H_{68}ClNO_{11}$ **FW:** 810.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A macrolactam that binds to macrophilin-12 and inhibits calcineurin as well as prolyl isomerase; the activation of T cells by allogeneic dendritic cells (IC_{50} = 0.55 nM) and suppresses the generation of pro-inflammatory cytokines; used in countering inflammatory skin diseases, such as eczema and psoriasis

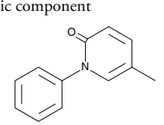
10 mg
50 mg
100 mg



Pirfenidone 13986

[53179-13-8] AMR 69, Deskar, Pirespa
MF: $C_{12}H_{11}NO$ **FW:** 185.2 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An orally active small molecule drug with antioxidant, anti-inflammatory, and anti-fibrotic effects; reduces inflammatory cytokine production, suppresses TGF-β expression, and lowers markers of oxidative stress; has effectiveness in IPF and other conditions with a significant fibrotic component

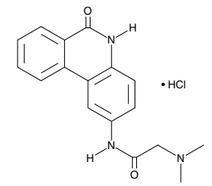
5 mg
10 mg
50 mg
100 mg



PJ-34 (hydrochloride) 14440

[344458-15-7]
MF: $C_{17}H_{17}N_3O_2$ • HCl **FW:** 331.8 **Purity:** ≥98%
A white to light brown powder **Stability:** ≥2 years at 4°C
Summary: An inhibitor of PARPs which can be used in cells or in animals; binds and inhibits the PARP TNKS1 (IC_{50} = 1 µM); inhibits MMP-2 when used at higher concentrations (IC_{50} = 56 µM)

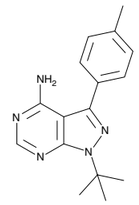
1 mg
5 mg
25 mg



PP1 (Src Inhibitor) 14244

[172889-26-8] AGL 1872, EI 275
MF: $C_{16}H_{19}N_5$ **FW:** 281.4 **Purity:** ≥98%
A white solid **Stability:** ≥2 years at -20°C
Summary: A potent, reversible, ATP-competitive, and selective inhibitor of the Src family of protein tyrosine kinases: $p56^{lck}$ (IC_{50} = 5 nM), $p59^{fynT}$ (IC_{50} = 6 nM), Hck (IC_{50} = 20 nM)

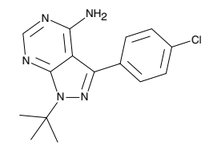
1 mg
5 mg



PP2 13198

[172889-27-9] AGL 1879
MF: $C_{15}H_{16}ClN_5$ **FW:** 301.8 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent, reversible, ATP-competitive, and selective inhibitor of the Src family of protein tyrosine kinases: $p56^{lck}$ (IC_{50} = 4 nM), $p59^{fynT}$ (IC_{50} = 5 nM), and Hck (IC_{50} = 5 nM)

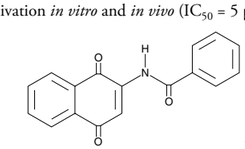
1 mg
5 mg
10 mg
25 mg



PPM-18 13327

[65240-86-0] NSC 73233
MF: $C_{17}H_{11}NO_3$ **FW:** 277.3 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An inhibitor of NF-κB activation *in vitro* and *in vivo* (IC_{50} = 5 µM)

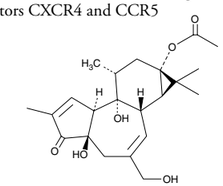
1mg
5 mg
10 mg
25 mg



Prostratin 10272

[60857-08-1] 13-O-Acetylphorbol, NSC 623310, SA 101A
MF: $C_{22}H_{30}O_6$ **FW:** 390.5 **Purity:** ≥98%
A solution in ethanol **Stability:** ≥1 year at -20°C
Summary: Potently induces HIV-1 reactivation in latent reservoirs of infected Jurkat-LAT-GFP cells (IC_{50} = ~0.5 µM); activates NF-κB *via* PKC and downregulates HIV-1 receptor CD4 expression and its co-receptors CXCR4 and CCR5

100 µg
250 µg
500 µg
1 mg



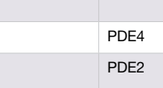
Phosphodiesterase Inhibitors

Item No.	Product Name	Inhibitory Target	Effective Concentration
10011135	BAY-60-7550	PDE2	IC_{50} = 2 nM (bovine) IC_{50} = 4.7 nM (human)
13183	CP 80633	PDE4	IC_{50} = 1.27 µM
13352	EHNA (hydrochloride)	PDE2	IC_{50} = 0.8 µM (human myocardium) IC_{50} = 2 µM (porcine myocardium) IC_{50} = 3.5 µM (rat hepatocyte) IC_{50} = 2 µM (human platelet)
13347	IBMX	Non-specific Inhibitor of cAMP and cGMP PGEs	
13624	Icariin	PDE5	IC_{50} = 5.9 µM
13357	Milrinone	PDE3A PDE3B	IC_{50} = 0.45 µM IC_{50} = 1.0 µM
14439	Obscurolide A_1	PDE1	IC_{50} = 15 mM
10011133	Papaverine	PDE activity	IC_{50} = 13 µM
10011132	Rolipram	PDE4	
10008671	Sildenafil	PDE5	IC_{50} = 3.6 nM (rabbit platelets) IC_{50} = 3 nM (human corpus cavernosum)
14008	Sildenafil Citrate	PDE5	IC_{50} = 3.6 nM (rabbit platelets) IC_{50} = 3 nM (human corpus cavernosum)
13939	Thiosildenafil	PDE5	
10010421	Zaprinast	PDE5 PDE6	IC_{50} = 0.5-0.76 µM IC_{50} = 15 µM

PX 12 14192

[141400-58-0]
MF: $C_7H_{12}N_2S_2$ **FW:** 188.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A competitive, irreversible inhibitor of Trx1; effective in suppressing the growth of cancer cells, with inhibition correlated with expression of Trx1 mRNA; reduces hypoxia-induced HIF-1α protein levels (IC_{50} = 7.2 µM) and expression of VEGF and iNOS; reduces microvessel density in MCF-7 tumor xenografts

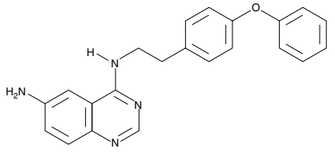
1 mg
5 mg
10 mg



QNZ 10006734

[545380-34-5] CAY10470
MF: $C_{22}H_{20}N_4O$ **FW:** 356.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An inhibitor of NF-κB activation with an IC_{50} value of 11 nM in human Jurkat cells; inhibits TNF-α production from LPS-stimulated mouse splenocytes (IC_{50} = 7 nM)

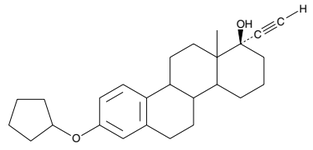
500 µg
1 mg
5 mg
10 mg



Quinestrol 10006320

[152-43-2] Estrovis®, Ethynyl Estradiol-3-cyclopentyl ether, W 3566
MF: $C_{25}H_{32}O_2$ **FW:** 364.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A synthetic estrogen that is effective in hormone replacement therapy; stored in adipose tissue, where it is slowly released and metabolized in the liver to its active form, ethynyl estradiol

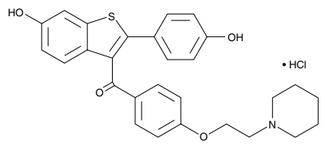
100 mg
250 mg
500 mg
1 g



Raloxifene (hydrochloride) 10011620

[82640-04-8] Evista®, Keoxifene, LY156758
MF: $C_{28}H_{27}NO_4S$ • HCl **FW:** 510.2 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A SERM that exhibits estrogenic activity in bone cells without stimulating breast or endometrial tissue

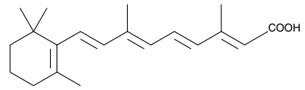
50 mg
100 mg
250 mg
500 mg



Retinoic Acid 11017

[302-79-4] all-trans Retinoic Acid, ATRA, NSC 122578, NSC 122758, Tretinoin, Vitamin A Acid
MF: $C_{20}H_{28}O_2$ **FW:** 300.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A metabolite of vitamin A that acts as a ligand for both the RAR and the RXR

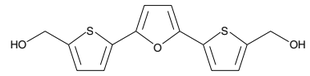
50 mg
100 mg
500 mg



RITA 10006426

[213261-59-7] 2,5-bis(5-hydroxymethyl-2-thienyl) Furan, NSC 652287
MF: $C_{14}H_{12}O_3S_2$ **FW:** 292.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An inhibitor of p53-HDM-2 interaction that can reactivate the tumor suppressor function of wild-type p53; binds to p53 with an apparent K_d value of 1.5 nM and prevents interaction with HDM-2 resulting in p53 stabilization, accumulation and activation

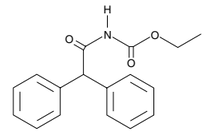
1 mg
5 mg
10 mg
50 mg



Ro 01-6128 11991

[302841-86-7]
MF: $C_{17}H_{17}NO_3$ **FW:** 283.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A positive allosteric modulator of metabotropic glutamate receptor 1 that potentiates glutamate-induced calcium release (EC_{50} = 104 nM), activates ERK1/2 phosphorylation (EC_{50} = 248 nM), and potentiates glutamate-induced cAMP production (EC_{50} = 21.5 µM)

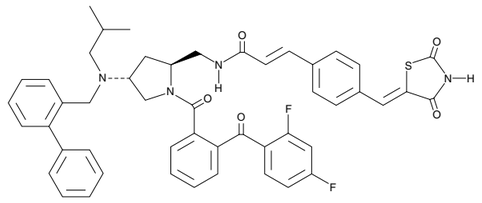
1 mg
5 mg
10 mg



RSC-3388 13343

[337307-06-9]
MF: $C_{49}H_{44}F_2N_4O_5S$ **FW:** 839.0 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A pyrrolidine derivative that potently inhibits $cPLA_2\alpha$, suppressing both recombinant human $cPLA_2$ *in vitro* (IC_{50} = 1.8 nM) and cellular PLA_2 activity in cells stimulated with the calcium ionophore A23187 (IC_{50} = 22 nM)

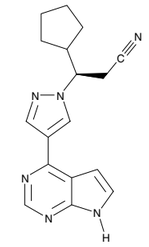
500 µg
1 mg
5 mg
10 mg



Ruxolitinib 11609

[941678-49-5] INCB 018424
MF: $C_{17}H_{18}N_6$ **FW:** 306.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent ATP mimetic that inhibits both JAK1 and JAK2 with IC_{50} values of 2.7 and 4.5 nM, respectively; blocks IL-6 signaling (IC_{50} = 281 nM) and proliferation of $JAK2^{V617F+}$ Ba/F3 cells (IC_{50} = 127 nM); reduces splenomegaly, decreases circulating levels of IL-6 and TNF-α, eliminates neoplastic cells, and prolongs survival in a mouse model of $JAK2^{V617F+}$ MPN

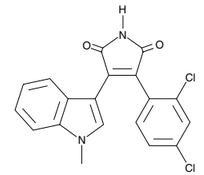
1 mg
5 mg
10 mg
25 mg



SB 216763 10010246

[280744-09-4]
MF: $C_{19}H_{12}Cl_2N_2O_2$ **FW:** 371.2 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An inhibitor of GSK3α (IC_{50} = 34 nM, GSK3β similar) that stimulates glycogen synthesis in Chang human liver cells (EC_{50} = 3.6 µM)

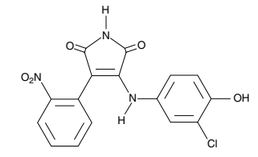
5 mg
10 mg
50 mg
100 mg



SB 415286 10010247

[264218-23-7]
MF: $C_{16}H_{10}ClN_3O_5$ **FW:** 359.7 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent and selective cell-permeable, ATP-competitive inhibitor of GSK3α (IC_{50} = 78 nM; K_i = 31 nM; similar potency for GSK3β)

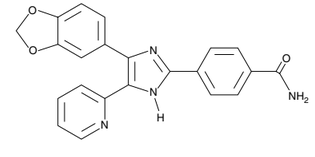
500 µg
1 mg
5 mg
10 mg



SB 431542 13031

[301836-41-9]
MF: $C_{22}H_{16}N_4O_3$ **FW:** 384.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent and selective inhibitor of the TGF-β1 receptor ALK5 (IC_{50} = 94 nM), ALK4 (IC_{50} = 140 nM) and, less effectively, ALK7; suppresses renewal in embryonic and induced pluripotent stem cells and promotes their differentiation

1 mg
5 mg
10 mg
25 mg



INTRANUCLEAR SIGNALING Pathways

by [Thomas G. Brock, Ph.D.]

The 'six degrees of separation' posits that every person is six acquaintances or less from every other person in the world. The idea insists that this is, indeed, a small world, characterized by a high degree of connectivity. Models of intracellular signaling can be compared with those illustrating the 'six degrees' theory. For example, prostaglandin E_2 (PGE_2) is separated from gene expression by five steps: binding to the EP_2 receptor, stimulation of adenylyl cyclase (AC), conversion of ATP to cAMP, activation of protein kinase A (PKA), and phosphorylation of cAMP response element-binding protein (CREB)(Figure 1). CREB is also linked to leukotriene B_4 (LTB_4), although gene expression through CREB is suppressed because LTB_4, through BLT1, blocks AC-mediated cAMP production. Note that, in this model, the nucleus is a distant target which only gets involved at the final step. However, extensive evidence supports the idea that, within the nucleus, second messengers are generated and control nuclear actions. This article touches on some of the intranuclear signaling pathways.

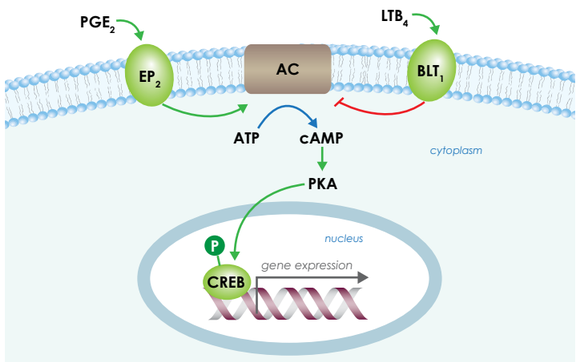


Figure 1. PGE_2 and LTB_4, as intercellular messengers, show 4 to 5 degress of separation from gene expression.

Nuclear Calcium Signaling

Calcium ions (Ca^{2+}) are key second messengers, maintained at sub-micromolar levels in the cytoplasm and nucleoplasm by ATP-dependent pumps. These pumps move Ca^{2+} to stores in the sarcoplasmic and endoplasmic reticula, as well as the nuclear envelope (which is contiguous with the rough ER), and out of the cell. When Ca^{2+} increases within the cell, it modulates a diverse array of enzymes, altering configuration and function. This action can interface with the nucleus at several levels. Increased cytoplasmic Ca^{2+} can activate PKC, calmodulin- (CaM-)dependent proteins like CaMKs, or the phosphatase calcineurin, initiating signaling that leads to nuclear import of other proteins, like ERK1/2, NF-κB, and NFAT. Furthermore, certain forms of PKC translocate into the nucleus upon activation. The Ca^{2+} activated diacylglycerol (DAG)-dependent PKCα moves into the nucleus in transiently-stimulated cells and in response to circadian cues. The atypical PKCδ, which is a Ca^{2+}-independent, DAG-dependent isoform, also moves to perinuclear membranes, as well as into the nucleus when stimulated.

An array of channels, both ligand-gated and voltage-gated, facilitates Ca^{2+}-selective transport.[1] A key type involved in receptor-mediated cell activation is the inositol trisphosphate (IP_3) receptor, which is triggered when $G_{q/11}$ protein-coupled receptors (GPCR) signal to phospholipase C (PLC) to cleave phosphatidylinositol 4,5-bisphosphate (PIP_2) to produce IP_3 and DAG. There are also DAG-activated Ca^{2+} channels. In normal conditions where modest levels of intercellular mediators are generated, ligand-activated G_qPCRs produce limited PLC action resulting in Ca^{2+} 'sparks' at the plasma membrane or ER (Figure 2). Ryanodine receptors are stimulated by intracellular Ca^{2+}. These may work in series with IP_3 receptors to produce Ca^{2+} 'waves', particularly in neurons.[2] Through either robust activation of multiple G_qPCRs or cooperative IP_3 receptor/ryanodine receptor action, Ca^{2+} waves may propagate throughout the cytoplasm and through nuclear pores into the nucleus.

Both IP_3 receptors and ryanodine receptors can be found in the nuclear envelope. The addition of the appropriate activators will induce nuclear Ca^{2+} mobilization, both in intact cells and in isolated nuclei. In addition, PLC exists in the nucleus as well as the cytoplasm in resting cells and can be induced to further accumulate in the nucleus in stimulated cells. Perhaps most surprisingly, a wide variety of GPCRs decorate the inner membrane of the nuclear envelope.[3] These include all of the different types of G proteins and their related subunits. As a result, all the components needed for ligand- and receptor-mediated changes in IP_3 and DAG, can be found in the nucleus. Thus, both localized intranuclear Ca^{2+} sparks as well as cross-nuclear waves can be produced. In addition, the inner membrane of the nuclear envelope has invaginations (a nucleoplasmic reticulum), increasing the internal surface area involved in Ca^{2+} signaling.[4] Perhaps more oddly, invaginations of the plasma membrane which extend toward or even into the nucleus can allow extracellular ligands to activate GPCRs and elevate nuclear Ca^{2+} levels.[5,6] Similar machinations permit changes in cAMP or active PKA within the nucleus.

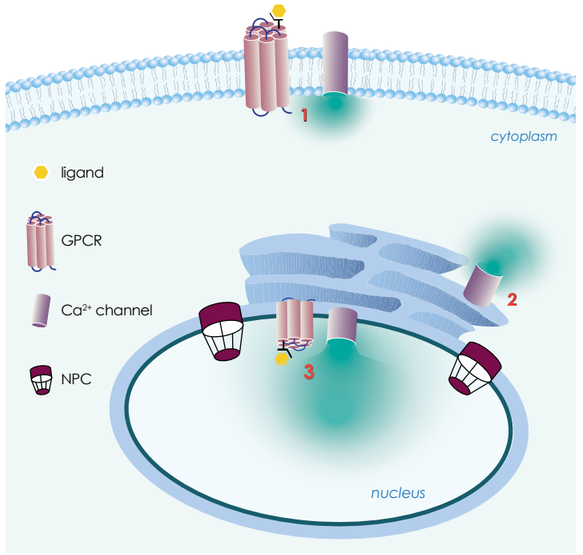


Figure 2. Ligand-activated G_qPCRs trigger Ca^{2+} sparks in different subcellular localizations: the plasma membrane (1), cytoplasmic reticulum (2), and inner nuclear envelope (3).

Like increases in cytoplasmic Ca^{2+}, those that occur within the nucleus have diverse effects, with fewer degrees of separation from gene expression. An increase in nuclear Ca^{2+} activates the transcription factor MEF2, releases the downstream regulatory element antagonist modulator (DREAM) from DNA, and stimulates CBP- and TORC-binding to CREB, thus altering gene expression.[5,6] In spinal neurons, nuclear Ca^{2+} signaling shifts the genomic program to control persistent inflammatory pain.[7] Less direct effects on transcription are mediated by Ca^{2+} interactions with histone-modifying proteins, high mobility group proteins, and transcriptional regulators. For example, nuclear Ca^{2+}, through CaMKII, controls phosphorylation of methyl CpG binding protein 2 (MeCP2), which modifies chromatin.[8]

Dynamic Nuclear Signaling

In physics, a body at rest tends to stay at rest, while a body in motion tends to stay in motion. In biology, neither seems to be the case. Biological systems contain multiple components which interface in many ways over space and time in dynamic fashion. One example involves the synthesis of leukotrienes (LTs), which are bioactive lipids involved primarily in intercellular signaling. The simple model is that LTs are biosynthesized from arachidonic acid (AA) by 5-lipoxygenase (5-LO), which makes the intermediate LTA_4. LTA_4 is converted to either the pro-inflammatory lipid LTB_4, by LTA_4 hydrolase, or the allergy/asthma mediator LTC_4, by LTC_4 synthase (Figure 3). In resting cells, 5-LO is soluble, but upon cell stimulation that leads to a rise in Ca^{2+}, 5-LO becomes activated and moves to nuclear and perinuclear membranes to initiate the conversion of AA to LTs. This can occur in a matter of seconds, so that a brief stimulation of leukocytes can lead to a rapid production and secretion of these powerful messengers, which move to neighboring cells to promote an inflammatory or allergic response.

A surprising number of proteins cycle into and out of the nucleus. 5-LO is one example. It has three independently regulated nuclear import signals which allow for different rates of nuclear accumulation, as well as a nuclear export signal. Signaling through cAMP/PKA results in phosphorylation of 5-LO, sequestration in the cytoplasm, and inhibition of LT synthesis.[9] On the other hand, phosphorylation by MK2 inhibits nuclear export but does not inhibit catalytic activity.[10,11] Phospholipases, including $cPLA_2$, liberate AA in the cytoplasm and fatty acid binding proteins carry AA into the nucleus.[9] While AA itself can bind and modulate a host of proteins, it is rapidly metabolized to LTA_4 by activated 5-LO. Importantly, other enzymes involved in LT metabolism have also been identified within the nucleus or in the nuclear envelope. Surprisingly, 5-LO synthesizes LTB_4 more effectively when it's in the nucleus than in the cytoplasm, based on mutations which alter 5-LO localization.[9] This indicates that these lipid messengers are abundantly produced within the nucleus. This has certain implications given that some LT receptors are found on nuclear membranes. Also, LTB_4 can directly active PPAR-α. Moreover, the electrophilic intermediate LTA_4 has been shown to form DNA and RNA adducts.[12] Thus, 5-LO, like PLC, is an enzyme that can move into the nucleus and generate signaling molecules.

More Notes on Nuclear Signaling

As noted above, abundant literature supports Ca^{2+} signaling within the nucleus. One direct source is nuclear PLC releasing IP_3 and DAG, leading to activation of IP_3 receptors at the nuclear envelope. While we are just beginning to appreciate the role of nuclear PLC/IP_3 action, it's clear that many enzymes involved in inositol phosphate metabolism shuttle between the nucleus and the cytoplasm, much like 5-LO.[13] The products, including IP_6, IP_7, and IP_8, are directly involved in gene regulation, chromatin remodeling, mRNA export, and DNA repair. Another example of nuclear import/export as a mechanism for regulating enzyme function is provided by class II histone deacetylases (HDACs), profiled elsewhere in this catalog (page 4).

Oxidant signaling also reaches into the nucleus. Certain cell stimulants, like UV radiation, trigger nuclear translocation of the redox regulators thioredoxin (Trx) and redox factor-1 (Ref-1).[14] Together, they regulate the transcriptional activity of several transcription factors, including AP-1, NF-κB, and HIF-1α. Also, hypoxia induces the movement of mitochondria along microtubules in capillary endothelial cells, resulting in clustering at the nucleus.[15] This is associated with an oxidant-rich nuclear environment which alters the expression of oxidant-sensitive genes, like VEGF. Additional detail regarding HIF signaling can be found on page 58. Certainly, the redox system must be active and important within the nucleus. This is an area that is ripe for additional research. n

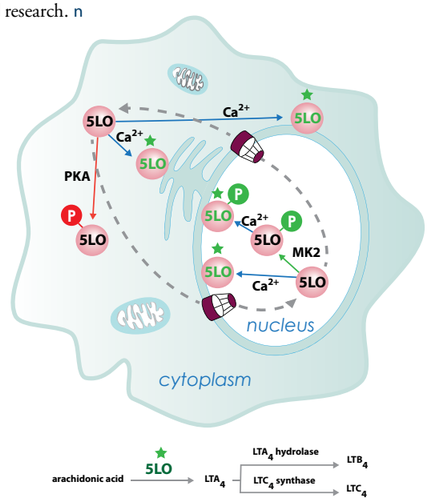


Figure 3. 5-LO shuttles into and out of the nucleus. In the cytoplasm, it is phosphorylated by PKA, which blocks import and inhibits activity. In the nucleus, 5-LO is phosphorylated by MK2, which inhibits nuclear export. In either location, Ca^{2+} induces membrane association of 5-LO and LT synthesis. In this way, 5-LO products can be made in either the cytoplasm or the nucleoplasm.

Reference List

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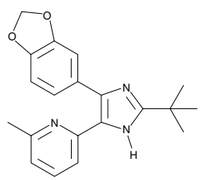
SB 505124 — 11793

[694433-59-5]
MF: $C_{20}H_{21}N_3O_2$ **FW:** 335.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: Inhibits ALK5- (IC_{50} = 47 nM), ALK4- (IC_{50} = 129 nM), and ALK7-dependent activation of downstream SMAD2 and SMAD3 and TGF-β-induced MAP kinase pathway components without altering ALK1-3, or ALK6-induced SMAD signaling

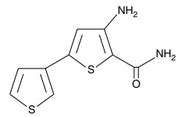
1 mg
5 mg
10 mg
25 mg



SC-514 — 10010267

[354812-17-2]
MF: $C_9H_8N_2OS_2$ **FW:** 224.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A selective and reversible inhibitor of IKK2 (IC_{50} = 3-12 µM) that displays >10-fold selectivity over 28 other kinases; attenuates NF-κB-mediated gene expression in synovial fibroblasts, smooth muscle cells, and astrocytes

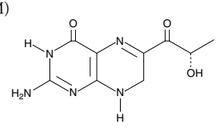
5 mg
10 mg
25 mg
50 mg



L-Sepiapterin — 81650

[17094-01-8]
MF: $C_9H_{11}N_5O_3$ **FW:** 237.2 **Purity:** ≥99%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A substrate for BH_4 synthesis *via* the pterin salvage pathway; inhibits rat liver GTP cyclohydrolase (IC_{50} = ~25 µM)

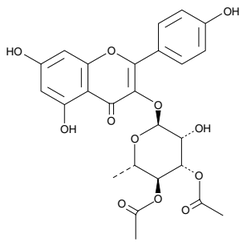
1 mg
5 mg
10 mg
50 mg



SL 0101-1 — 11704

[77307-50-7]
MF: $C_{25}H_{24}O_{12}$ **FW:** 516.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A kaempferol glycoside that selectively inhibits RSK2 with an IC_{50} value of 89 nM (K_i = 1 µM) without interfering with upstream activators of RSK, including ERK, MEK, EGFR, and PKC; inhibits the proliferation of MCF-7 breast cancer cells at 100 µM and attenuates angiotensin II-induced cell proliferation at 30 µM

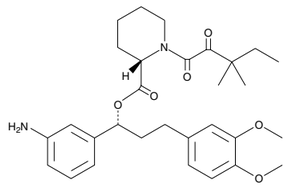
500 µg
1 mg
5 mg



SLF — 10007974

Synthetic Ligand of FKBP
MF: $C_{30}H_{40}N_2O_6$ **FW:** 524.7 **Purity:** ≥98%
A solution in methyl acetate **Stability:** ≥1 year at -20°C
Summary: A cell-permeable analog of FK-506 that binds tightly to FKBP but lacks the ability to inhibit calcineurin

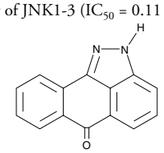
5 mg
10 mg
50 mg
100 mg



SP 600125 — 10010466

[129-56-6] NSC 75890, 1PMV, Pyrazolanthrone
MF: $C_{14}H_8N_2O$ **FW:** 220.2 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent and reversible inhibitor of JNK1-3 (IC_{50} = 0.11 µM)

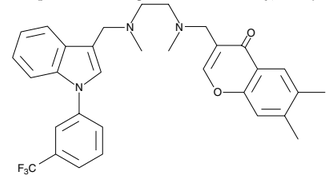
5 mg
10 mg
25 mg
50 mg



SPD-304 — 10008012

[869998-49-2]
MF: $C_{32}H_{32}F_3N_3O_2$ **FW:** 547.6 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An inhibitor of TNF-α that prevents binding to the TNFR1 (IC_{50} = 22 µM)

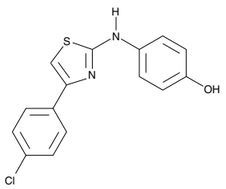
500 µg
1 mg
5 mg
10 mg



Sphingosine Kinase Inhibitor 2 — 10009222

[312636-16-1] SKI II, SPHK I2
MF: $C_{15}H_{11}ClN_2OS$ **FW:** 302.8 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent, selective inhibitor of SPHK 1 (IC_{50} = 0.5 µM); inhibits proliferation of several human cancer cell lines with IC_{50} values in the low µM range (0.9-4.6 µM)

5 mg
10 mg
25 mg
50 mg

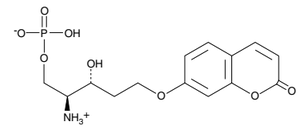


Sphingolipids	
Item No.	**Product Name**
10007945	D-*erythro*-Sphinganine
10007901	D-*erythro*-Sphingosine C-15
10007902	D-*erythro*-Sphingosine C-17
10007903	D-*erythro*-Sphingosine C-20
10010541	L-*threo*-Sphingosine C-18
62570	Sphingosine-1-Phosphate
10007947	Lyso-Sphingomyelin

Sphingosine-1-Phosphate Lyase Fluorogenic Substrate — 13238

S1P Lyase Fluorogenic Substrate
MF: $C_{14}H_{18}NO_8P$ **FW:** 359.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥1 year at -20°C
Summary: A substrate of S1P lyase, leading to the production of the fluorescent product umbelliferone; intended to be used to monitor or measure S1P lyase activity

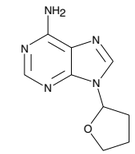
1 mg
5 mg
10 mg



SQ 22,536 — 13339

[17318-31-9] NSC 53339
MF: $C_9H_{11}N_5O$ **FW:** 205.2 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An inhibitor of adenylyl cyclase (IC_{50} = 13 µM) that inhibits PGE_1-stimulated increases in cAMP levels in intact platelets; used to evaluate adenylyl cyclase activity during iloprost-induced vasorelaxation, inhibiting cAMP elevation (100-300 µM) without effecting relaxation

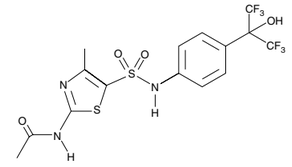
5 mg
10 mg
25 mg
50 mg



SR 1001 — 10922

MF: $C_{15}H_{13}F_6N_3O_4S_2$ **FW:** 477.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A synthetic ligand specific for RORα and RORγ (K_is = 172 and 111 nM, respectively) that functions as an inverse agonist; inhibits T_H17 cell differentiation and IL-17A secretion in cultured splenocytes and human peripheral blood mononuclear cells at 5 µM; 25 mg/kg twice/day delays onset and severity of experimental autoimmune encephalomyelitis, a mouse model of multiple sclerosis

1 mg
5 mg
10 mg
25 mg



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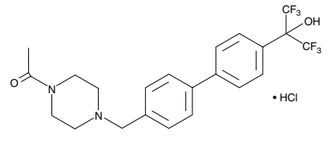
SR 1555 (hydrochloride) — 12071

MF: $C_{22}H_{22}F_6N_2O_2$ • HCl **FW:** 496.9 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A selective ligand of RORγ (IC_{50} = 1 µM); does not bind RORα, LXR, or FXR; acts as an inverse agonist of RORγ, inhibiting endogenous IL-17A gene expression and suppressing differentiation of T_H17 cells; stimulates T regulatory development

1 mg
5 mg
10 mg
25 mg

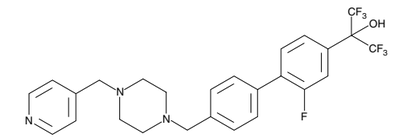


NOTE: Sold under license from The Scripps Research Institute

SR 2211 — 11972

[1359164-11-6]
MF: $C_{26}H_{24}F_7N_3O$ **FW:** 527.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: Selectively binds RORγ (K_i = 105 nM), acting as an inverse agonist of constitutive *in vitro* RORγ activity (IC_{50} = 320 nM); significantly inhibits gene expression of IL-17 and IL-23 receptor in activated EL-4 mouse T lymphocytes when given at 5 µM

1 mg
5 mg
10 mg

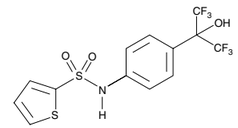


NOTE: Sold under license from The Scripps Research Institute

SR 3335 — 12072

[293753-05-6] ML 176
MF: $C_{13}H_9F_6NO_3S_2$ **FW:** 405.3 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A selective inverse agonist of RORα, competitively inhibiting the binding of 25-hydroxycholesterol to the ligand binding domain (K_i = 220 nM) and inhibiting constitutive transactivation activity (IC_{50} = 480 nM); evokes RORα-dependent effects both *in vitro* and *in vivo*

1 mg
5 mg
10 mg
25 mg



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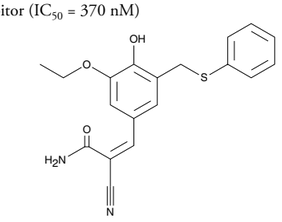
ST638 — 13337

[107761-24-0]
MF: $C_{19}H_{18}N_2O_3S$ **FW:** 354.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A tyrosine kinase inhibitor (IC_{50} = 370 nM)

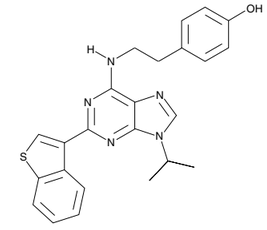
1 mg
5 mg
10 mg
25 mg



StemRegenin 1 — 10625

[1227633-49-9] SR1
MF: $C_{24}H_{23}N_5OS$ **FW:** 429.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A purine derivative that reversibly antagonizes AhR signaling (IC_{50} = 127 nM in $CD34^+$ cells); induces a 50-fold increase in human embryonic stem cells expressing CD34 (EC_{50} = 120 nM) and a 17-fold increase in stem cells that retain the ability to engraft immunodeficient mice

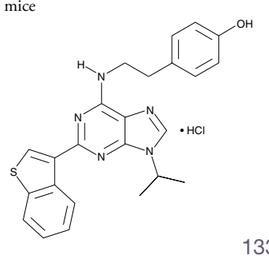
1 mg
5 mg
10 mg



StemRegenin 1 (hydrochloride) 14268

SR1
MF: $C_{24}H_{23}N_5OS \bullet HCl$ **FW:** 466.0 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A purine derivative that reversibly antagonizes AhR signaling (IC_{50} = 127 nM in $CD34^+$ cells); induces a 50-fold increase in human embryonic stem cells expressing CD34 (EC_{50} = 120 nM) and a 17-fold increase in stem cells that retain the ability to engraft immunodeficient mice

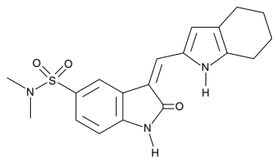
1 mg
5 mg
10 mg



SU 6656 13338

[330161-87-0]
MF: $C_{19}H_{21}N_3O_3S_2$ **FW:** 371.5 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A selective inhibitor of Src kinases, including Src, Yes, Lyn, and Fyn (IC_{50} = 280, 20, 130, and 170 nM, respectively

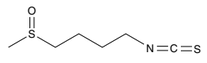
1 mg
5 mg
10 mg
25 mg



Sulforaphane 10496

[4478-93-7]
MF: $C_6H_{11}NOS_2$ **FW:** 177.3 **Purity:** ≥98%
A solution in ethanol **Stability:** ≥1 year at -20°C
Summary: An isothiocyanate that potently induces chemopreventative enzymes *via* Keap1-Nrf2 signaling and ARE-driven gene expression; at 15 µM, inhibits class I and II HDAC activity and suppresses tumor growth selectively in cancerous prostate epithelial cells without affecting normal cells

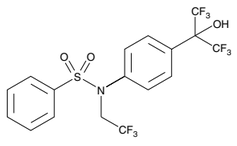
5 mg
10 mg
25 mg



T0901317 71810

[293754-55-9]
MF: $C_{17}H_{12}F_9NO_3S$ **FW:** 481.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥1 year at -20°C
Summary: A potent and selective agonist for both LXRα and LXRβ (EC_{50} = 50 nM)

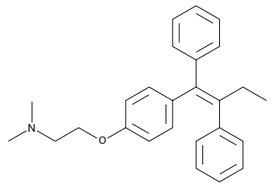
5 mg
10 mg
50 mg
100 mg



Tamoxifen 13258

[10540-29-1]
MF: $C_{26}H_{29}NO$ **FW:** 371.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A selective ER modulator; an ER antagonist in breast tissue, effective in treating early breast cancer; an ER agonist in bone and blood vessels and a partial ER agonist in uterine tissues

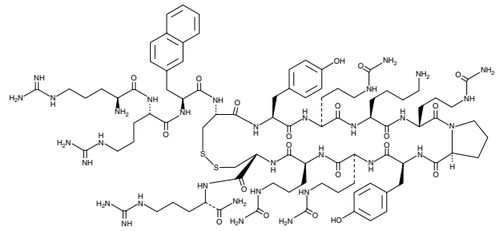
500 mg
1 g
5 g
10 g



TC 14012 11974

[368874-34-4]
MF: $C_{90}H_{140}N_{34}O_{19}S_2$ **FW:** 2,066.4 **Purity:** ≥95%
A crystalline solid **Stability:** ≥1 year at -20°C
Summary: An antagonist of CXCR4, blocking CXCR4-mediated HIV infection with an IC_{50} value of 19.3 nM; at 100 µg/ml, inhibits CXCL12-induced phosphorylation of p42/44 MAPK and STAT3; activates CXCR7 (EC_{50} = 350 nM), resulting in the recruitment of β-arrestin and ERK1/2 phosphorylation

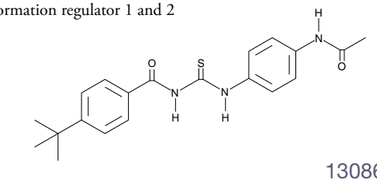
1 mg
5 mg
10 mg



Tenovin-1 13085

[380315-80-0]
MF: $C_{20}H_{23}N_3O_2S$ **FW:** 369.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A small molecule activator of p53 that decreases the growth of BL2 Burkitt's lymphoma and ARN8 melanoma cells; inhibits the deacetylase activity of purified human silent information regulator 1 and 2

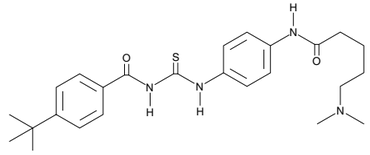
5 mg
10 mg
50 mg
100 mg



Tenovin-6 13086

[1011557-82-6]
MF: $C_{25}H_{34}N_4O_2S$ **FW:** 454.6 **Purity:** ≥95%
A crystalline solid **Stability:** ≥1 year at -20°C
Summary: An analog of tenovin-1; elevates p53 activity in MCF-7 cells at 10 µM and reduces growth of ARN8 melanoma xenograft tumors in SCID mice at a dose of 50 mg/kg

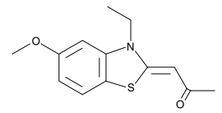
1 mg
5 mg
10 mg
25 mg



TG003 10398

[300801-52-9]
MF: $C_{13}H_{15}NO_2S$ **FW:** 249.3 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A novel benzothiazole compound that inhibits Clk1/Sty and Clk4 (IC_{50} = 20 and 15 nM, respectively); at 1 µM, suppresses Clk-mediated phosphorylation which inhibits SF2/ASF-dependent splicing of β-globin pre-mRNA *in vitro*

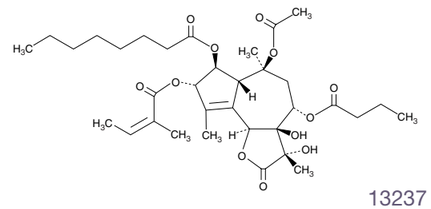
1 mg
5 mg
10 mg
25 mg



Thapsigargin 10522

[67526-95-8]
MF: $C_{34}H_{50}O_{12}$ **FW:** 650.8 **Purity:** ≥97%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A non-competitive, cell permeable inhibitor of calcium transport by SERCAs (IC_{50} values are cell type-dependent and range from ~2-80 nM); increases intracellular calcium, leading to cell activation, histamine release, and increased cell proliferation; has anti-inflammatory and anticancer effects *in vivo*

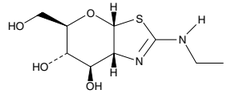
1 mg
5 mg



Thiamet G 13237

[1009816-48-1]
MF: $C_9H_{16}N_2O_4S$ **FW:** 248.3 **Purity:** ≥97%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent and selective inhibitor of O-GlcNAcase (K_i = 21 nM); increases cellular O-GlcNAc-modified protein levels (EC_{50} = 30 nM) and blocks phosphorylation of tau protein both in cultured PC-12 cells and in rats (200 mg/kg/day); is orally bioavailable and effectively cross the blood brain barrier

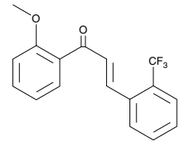
1 mg
5 mg
10 mg



2-Trifluoromethyl-2'-methoxychalcone 11881

[1309371-03-6]
MF: $C_{17}H_{13}F_3O_2$ **FW:** 306.3 **Purity:** ≥98%
A solution in methyl acetate **Stability:** ≥1 year at -20°C
Summary: A potent activator of Nrf2-regulated activity, both, *in vitro* (10 µM) and in mice (50 mg/kg)

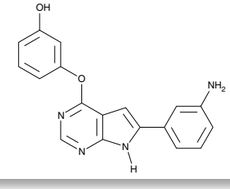
5 mg
10 mg
50 mg
100 mg



TWS119 10011251

[601514-19-6]
MF: $C_{18}H_{14}N_4O_2$ **FW:** 318.3 **Purity:** ≥90%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent inhibitor of GSK3β (IC_{50} = 30 nM) that induces neurogenesis in mouse embryonic stem cells

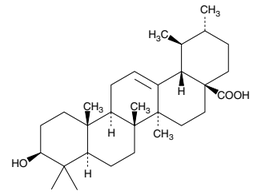
1 mg
5 mg
10 mg
25 mg



Ursolic Acid 10072

[77-52-1] Bungeolic Acid, Maerotaine, Malol, NSC 4060, NSC 167406, Prunol
MF: $C_{30}H_{48}O_3$ **FW:** 456.7 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A natural triterpenoid carboxylic acid that is known to have antioxidative, antimicrobial, anti-inflammatory, and anticancer activities; inhibits Na^+/K^+-ATPase activity (IC_{50} = 24.7 µM) and blocks NF-κB activation in various human cancer cells lines (10-100 µM), inhibiting cell proliferation and inducing apoptosis

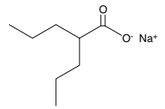
50 mg
100 mg
250 mg



Valproic Acid (sodium salt) 13033

[1069-66-5] 2-Propylvaleric Acid, Sodium Valproate
MF: $C_8H_{15}O_2 \bullet Na$ **FW:** 166.2 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An analog of valeric acid, long used as an anti-convulsant; inhibits Class I HDACs with an IC_{50} value of ~2 mM; also inhibits GSK3 and depletes cellular 1,4,5-IP_3

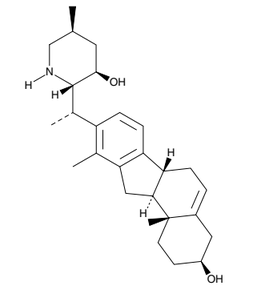
10 g
25 g
50 g
100 g



Veratramine 11724

[60-70-8] NSC 17821, NSC 23880
MF: $C_{27}H_{39}NO_2$ **FW:** 409.6 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An analog of cyclopamine that inhibits the Hh signaling-dependent proliferation of NIH/3T3 cells at 8 µM and dose dependently inhibits platelet aggregation in rabbits *ex vivo*; induces serotonin release and inhibits its re-uptake in the central nervous system

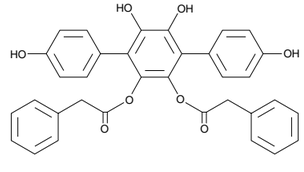
5 mg
10 mg
25 mg
50 mg



Vialinin A 10010519

[858134-23-3] Terrestrin A
MF: $C_{34}H_{26}O_8$ **FW:** 562.6 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A natural compound with strong antioxidant activity; potently inhibits the release of TNF-α (IC_{50} = 0.09 nM) and IL-4 (IC_{50} = 2.8 nM), as well as β-hexosaminidase and CCL2 (MCP-1) from IgE-stimulated RBL-2H3 mast cells

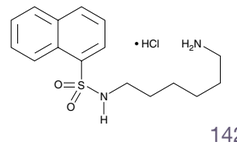
1 mg
5 mg
10 mg
25 mg



W-5 (hydrochloride) 14271

[61714-25-8]
MF: $C_{16}H_{22}N_2O_2S$ • HCl **FW:** 342.9 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A less active, chlorine-deficient analog of W-7, the potent calmodulin antagonist (K_i = 11 µM); suitable for use as a control compound for understanding the specificity of other calmodulin antagonists

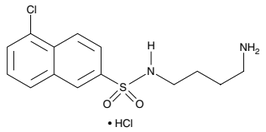
5 mg
25 mg



W-13 (hydrochloride) 14277

[88519-57-7]
MF: $C_{14}H_{17}ClN_2O_2S$ • HCl **FW:** 349.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent antagonist of calmodulin (IC_{50} = 22 µM) that is widely used to investigate Ca^{2+}/calmodulin-regulated enzyme activities

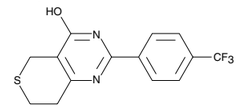
1 mg
5 mg
10 mg



XAV939 13596

[284028-89-3]
MF: $C_{14}H_{11}F_3N_2OS$ **FW:** 312.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A small molecule inhibitor of tankyrase 1 and 2 (IC_{50} = 11 and 4 nM, respectively); increases the protein levels of the axin-GSK3β complex and promotes the degradation of β-catenin; inhibits colony formation of adenomatous polyposis coli-deficient colorectal cancer cells at 0.33 µM

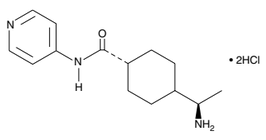
1 mg
5 mg
10 mg
25 mg



Y-27632 (hydrochloride) 10005583

[129830-38-2]
MF: $C_{14}H_{21}N_3O$ • 2HCl **FW:** 320.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent, ATP-competitive inhibitor of ROCK including p160ROCK (K_i = 140 nM) and ROCK-II (IC_{50} = 800 nM); also inhibits PRK2 with an IC_{50} value of 600 nM

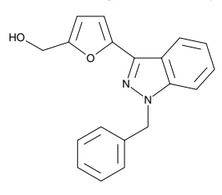
500 µg
1 mg
5 mg
10 mg



YC-1 81560

[170632-47-0]
MF: $C_{19}H_{16}N_2O_2$ **FW:** 304.3 **Purity:** ≥99%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An NO-independent activator of soluble guanylyl cyclase; increases the activity of purified soluble guanylyl cyclase with an ED_{50} value of 20 µM in the absence of NO

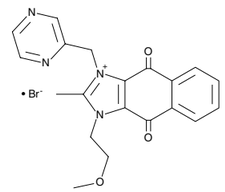
1 mg
5 mg
10 mg
50 mg



YM55 11490

[781661-94-7] Sepantronium bromide
MF: $C_{20}H_{19}N_4O_3$ • Br **FW:** 443.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A small molecule that suppresses transactivation of survivin through direct binding to its promoter; induces apoptosis in p53-deficient cancer cells *in vitro* at 10 nM with little effect on expression levels of other IAP- or Bcl-2-related proteins

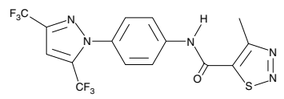
1 mg
5 mg
10 mg
25 mg



YM-58483 13246

[223499-30-7] BTP 2
MF: $C_{15}H_9F_6N_5O_5$ **FW:** 421.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent inhibitor of calcium release-activated calcium channels in lymphocytes (IC_{50} = 100 nM); also inhibits lung IL-4 and CysLT generation in animal models of asthma

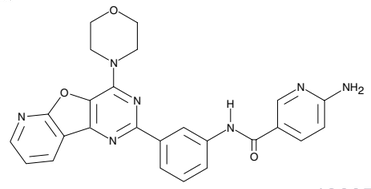
1 mg
5 mg
10 mg
25 mg



YM-201636 13576

[371942-69-7]
MF: $C_{25}H_{21}N_7O_3$ **FW:**467.5 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A cell-permeable and selective inhibitor of PIKfyve (IC_{50} = 33 nM); reversibly impairs endosomal trafficking in NIH3T3 cells and blocks retroviral exit by budding from cells; inhibits basal and insulin-activated 2-deoxyglucose uptake (IC_{50} = 54 nM) in adipocytes

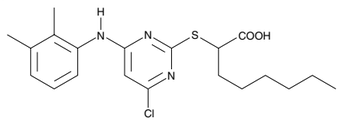
1 mg
5 mg
10 mg



YS121 13665

[916482-17-2]
MF: $C_{20}H_{26}ClN_3O_2S$ **FW:** 408.0 **Purity:** ≥98%
A solution in methyl acetate **Stability:** ≥1 year at -20°C
Summary: A dual inhibitor of mPGES-1 (IC_{50} = 3.9 µM) and 5-LO (IC_{50} = 4.1 µM); blocks PGE_2 and LT synthesis in cell free and intact cell assays, and also in an animal model of inflammation

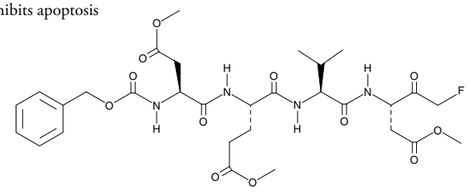
1 mg
5 mg
10 mg
25 mg



Z-DEVD-FMK 14414

[210344-95-9]
MF: $C_{30}H_{41}FN_4O_{12}$ **FW:** 668.7 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A cell-permeable irreversible inhibitor of caspase-3 (IC_{50} = 130 nM); potently inhibits apoptosis

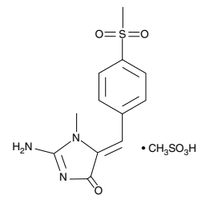
500 µg
1 mg
5 mg



ZLJ-6 13271

[1051931-39-5]
MF: $C_{12}H_{13}N_3O_3S$ • CH_3SO_3H **FW:** 375.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A dual inhibitor of COX and 5-LO enzymes (IC50 = 0.73, 0.31, and 0.99 µM for COX-1, COX-2, and 5-LO, respectively, in whole blood)

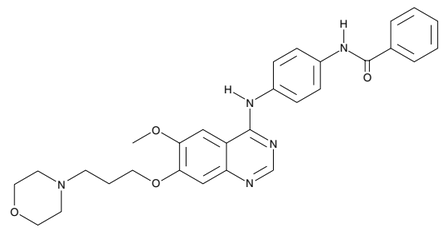
1 mg
5 mg
10 mg
25 mg



ZM 447439 13601

[331771-20-1]
MF: $C_{29}H_{31}N_5O_4$ **FW:** 513.6 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A selective inhibitor of Aurora B kinase (IC_{50} = 10 µM), less potently inhibiting Aurora C and A (IC_{50} = 250 and 1,000 nM, respectively); has been used to study the role of Aurora B in molecular events associated with mitosis and cytokinesis; selectively inhibits proliferating cells rather than non-dividing cells

5 mg
10 mg
50 mg

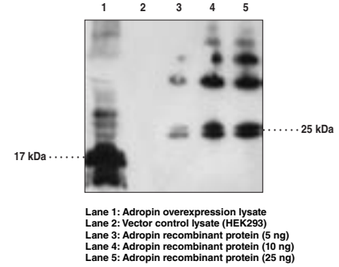


Antibodies

Adropin Polyclonal Antibody 10381

Energy Homeostasis-Associated Protein
Peptide affinity-purified IgG **Stability:** ≥2 years at -20°C
Summary: Antigen: human adropin amino acids 34-76 • Host: rabbit • Cross Reactivity: (+) human adropin • Application(s): ELISA and WB • Adropin, encoded by the energy homeostasis associated gene, is involved in glucose homeostasis and lipid metabolism. It is involved in post-transcriptional activation of eNOS, the up-regulation of VEGFR2, and activation of the ERK1/2 pathway.

1 ea



Lane 1: Adropin overexpression lysate
Lane 2: Vector control lysate (HEK293)
Lane 3: Adropin recombinant protein (5 ng)
Lane 4: Adropin recombinant protein (10 ng)
Lane 5: Adropin recombinant protein (25 ng)

AIF Polyclonal Antibody 160773

Apoptosis-Inducing Factor, Programmed Cell Death Protein 8
Peptide affinity-purified IgG **Stability:** ≥2 years at -20°C
Summary: Antigen: human AIF amino acids 151-180 • Host: rabbit • Cross Reactivity: (+) human, rat, and mouse AIF • Application(s): WB • AIF is a highly conserved mitochondrial protein with roles in redox-biochemistry and apoptosis.

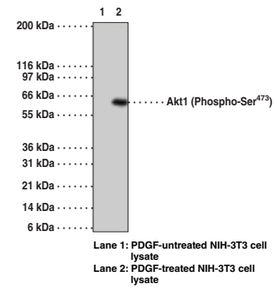
500 µl

•Also Available: **AIF Blocking Peptide** (360773)

Akt1 (Phospho-Ser^{473}) Monoclonal Antibody (Clone 104A282) 13733

Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human Akt1 containing phospho-serine^{473} • Host: mouse, clone 104A282 • Isotype: $IgG_{2κ}$ • Cross Reactivity: (+) human and mouse Akt1 • Application(s): IP and WB • Akt/PKB is a serine/threonine kinase that mediates cell survival and is thought to be a critical factor in the genesis of cancer. The major phosphorylation sites required for activation are Thr^{308} and Ser^{473}.

1 ea

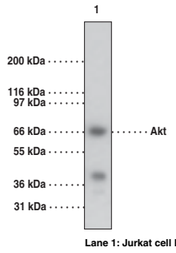


Lane 1: PDGF-untreated NIH-3T3 cell lysate
Lane 2: PDGF-treated NIH-3T3 cell lysate

Akt1 Polyclonal Antibody 13732

Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human Akt1 amino acids 464-477; this peptide sequence is identical in human, mouse, chicken, and frog • Host: rabbit • Cross Reactivity: (+) human Akt1 • Application(s): WB • Akt/PKB is a serine/threonine kinase involved in many cellular signaling pathways and acts as a transducer of many functions initiated by growth factor receptors that activate PI3-kinase.

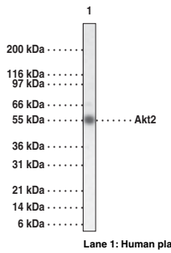
1 ea



Akt2 Monoclonal Antibody (Clone 95C567.1.2) 13734

Ascites fluid **Stability:** ≥1 year at -20°C
Summary: Antigen: human Akt2 amino acids 106-123 • Host: mouse, clone 95C657.1.2 • Isotype: IgM • Cross Reactivity: (+) human Akt2 • Application(s): WB • Akt2 is a serine/threonine kinase involved in some human cancers and an important signaling molecule in the insulin signaling pathway.

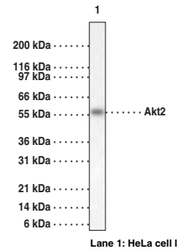
1 ea



Akt2/3 Polyclonal Antibody 13735

Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human Akt2 amino acids 319-331; this sequence is 100% homologus in Akt3 • Host: rabbit • Cross Reactivity: (+) human Akt2/3 • Application(s): WB • Akt/PKB is a serine/threonine kinase involved in some human cancers and an important signaling molecule in the insulin signaling pathway. There are three known isoforms of this enzyme in mammalian cells (1-3).

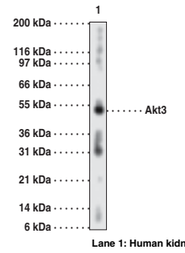
1 ea



Akt3 Monoclonal Antibody (Clone 66C1247.1) 13736

Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human Akt3 amino acids 119-136; this sequence is identical in human, mouse, rat, sheep, dog, and chicken • Host: mouse, clone 66C1247.1 • Isotype: IgG_1 • Cross Reactivity: (+) human, mouse, and rat Akt3 • Application(s): WB • Akt/PKB is a serine/threonine kinase which is involved in many cellular signaling pathways and acts as a transducer of many functions initiated by growth factor receptors that activate PI3-kinase. Akt3 is a kinase predominantly expressed in the brain.

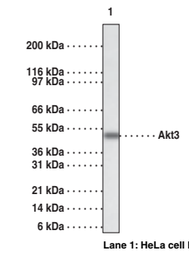
1 ea



Akt3 Polyclonal Antibody 13737

Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: synthetic peptide from human Akt3 amino acids 119-136; this sequence is identical in human, mouse, and rat • Host: rabbit • Cross Reactivity: (+) human, mouse, and rat Akt3 • Application(s): WB • Akt/PKB is a serine/threonine kinase which is involved in many cellular signaling pathways and acts as a transducer of many functions initiated by growth factor receptors that activate PI3-kinase. Akt3 is a kinase predominantly expressed in the brain.

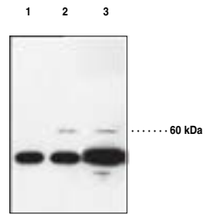
1 ea



Apaf-1 Polyclonal Antibody 160780

Apoptosis Protease-Activating Factor 1
Peptide affinity-purified IgG **Stability:** ≥1 year at 4°C
Summary: Antigen: human Apaf-1 amino acids 12-28; the sequence of the peptide is identical between human and mouse • Host: rabbit • Cross Reactivity: (+) human and mouse Apaf-1 • Application(s): WB • Apaf-1 binds to cytochrome c (Apaf-2) and caspase-9 (Apaf-3), which leads to caspase-9 activation. Activated caspase-9 in turn cleaves and activates caspase-3, one of the key proteases responsible for the proteolytic cleavage of many key proteins in apoptosis. It can also associate with caspase-4 and -8.

100 µg

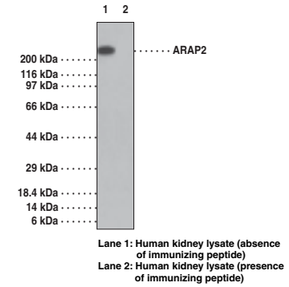


•Also Available: **Apaf-1 Blocking Peptide** (360780)

ARAP2 Polyclonal Antibody 13495

Centaurin-δ-1
Protein A-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human ARAP2 within the region of amino acids 1,670-1,720 • Host: rabbit • Cross Reactivity: (+) human ARAP2 • Application(s): IHC and WB • ARAP2 is a PIP_3-dependent GTPase-activating protein that binds to RhoA-GTP, and modulates actin cytoskeleton remodeling by regulating ARF and RHO family members. ARAP2 associates with focal adhesions and functions downstream of RhoA to regulate focal adhesion dynamics.

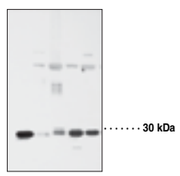
1 ea



ARC Polyclonal Antibody 160737

Apoptosis Repressor with CARD
Affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human ARC amino acids 191-208 • Host: rabbit • Cross Reactivity: (+) human and mouse ARC • Application(s): IP and WB • ARC interacts with caspase-2 and -8 and inhibits enzymatic activity of caspase-8. ARC suppresses apoptosis induced by cell death adapters FADD and TRADD and by cell death receptors Fas, TNFR-1, and DR3.

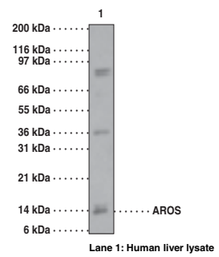
1 ea



AROS Polyclonal Antibody (aa 1-50) 13496

Protein A-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: synthetic peptide from human AROS within the region of amino acids 1-50 • Host: rabbit • Cross Reactivity: (+) human AROS • Application(s): WB • AROS interacts with extraribosomal protein RPS19, playing a role in the signaling pathways that regulate rRNA transcription.

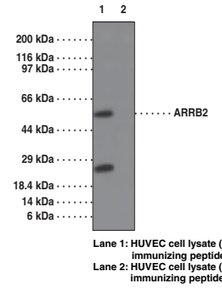
1 ea



ARRB2 Polyclonal Antibody 13498

β-Arrestin-2
Peptide affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: peptide from human ARRB2 within the region of amino acids 15-50 • Host: rabbit • Cross Reactivity: (+) ovine, canine, equine, human, monkey, mouse, and rat ARRB2 • Application(s): IHC (paraffin-embedded sections) and WB • ARRB2 is an adaptor protein involved in heterotrimeric GPCR desensitization. It is known to regulate β-adrenergic receptor A function, thus enhancing β2AR receptor mediated nuclear translocation of ERK. Along with AIP4, ARRB2 acts as an endosomal sorting molecule that mediates CXCR4 entry into a degradative pathway.

1 ea



ATF2 (Phospho-Ser^{490,498}) Polyclonal Antibody 10009410

Activating Transcription Factor 2
Peptide affinity-purified antibody **Stability:** ≥1 year at -20°C
Summary: Antigen: phosphopeptide corresponding to amino acid residues surrounding phospho-Ser^{490,498} of human ATF2 • Host: rabbit • Cross Reactivity: (+) human ATF2; expected to react with rat ATF2 • Application(s): IHC (frozen sections) and WB • ATF2 binds to both AP-1 and CRE DNA response elements and is a member of the ATF/CREB family of leucine zipper proteins. It has been implicated in the transcriptional regulation of a number of genes including cytokines, cell cycle control, and apoptosis.

100 µl

Bim/BOD (IN) Polyclonal Antibody 10011385

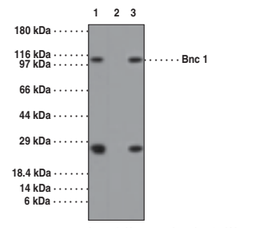
Immunoaffinity chromatography purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: internal central human Bim amino acids • Host: rabbit • Cross Reactivity: (+) human, mouse, and rat Bim/BOD (IN) • Application(s): IHC and WB • Bim/BOD interacts with diverse members in the pro-survival Bcl-2 sub-family including Bcl-2, -xL, and -w and induces apoptosis.

25 µg
100 µg

Bnc 1 Polyclonal Antibody 13502

Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: peptide from human Bnc 1 within the region of amino acids 330-380 • Host: rabbit • Cross Reactivity: (+) chimpanzee, human, and monkey Bnc 1 • Application(s): WB • Bnc 1 is a 994 amino acid transcription factor specific for squamous epithelium and for the constituent keratinocytes at a stage either prior to or at the very beginning of terminal differentiation.

1 ea



CaMKII Monoclonal Antibody (Clone 6G9) 10011437

Calcium/Calmodulin-dependent Protein Kinase II
Protein G-purified mouse IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: rat recombinant CaMKII • Host: mouse, clone 6G9 • Isotype: IgG_1 • Cross Reactivity: (+) mouse, rat, and bovine CaMKII • Application(s): ELISA, IF, IHC, IP, and WB • CaMKII functions in neural synaptic stimulation and T cell receptor signaling.

25 µg
100 µg

CaMKII (phospho-Thr^{286}/Thr^{287}) Monoclonal Antibody (Clone 22B1) 10011438

Calcium/Calmodulin-dependent Protein Kinase II
Protein G-purified mouse IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: synthetic peptide • Host: mouse, clone 22B1 • Isotype: IgG_1 • Cross Reactivity: (+) rat CaMKII • Application(s): ELISA, IF, IP, and WB • CaMKII functions in neural synaptic stimulation and T cell receptor signaling. The binding of Ca^{2+}/calmodulin to its regulatory domain releases its auto inhibitory effect and activates the kinase. This kinase activation results in autophosphorylation at Thr^{286}. PP1 dephosphorylates phospho-CaMKII at Thr^{286} and PKA prevents this dephosphorylation.

25 µg
100 µg

CREB (Phospho-Ser^{133}) Polyclonal Antibody 10009181

Affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: phosphopeptide corresponding to amino acid residues surrounding the phospho-Ser^{133} of rat CREB • Host: rabbit • Cross Reactivity: (+) rat CREB • Application(s): WB • CREB is one of the best characterized stimulus-induced transcription factors. This transcription factor is a component of intracellular signaling events that regulate a wide range of biological functions, from spermatogenesis to circadian rhythms and memory. A variety of protein kinases including PKA, MAPKs, and CaMKs phosphorylate CREB at Ser1^{33}, which is required for CREB-mediated transcription.

1 ea

DARPP-32 (Phospho-Thr^{34}) Polyclonal Antibody 10603

Peptide affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: phosphopeptide corresponding to amino acid residues surrounding phospho-Thr^{34} of rat DARPP-32 • Host: rabbit • Cross Reactivity: (+) rat DARPP-32 • Application(s): WB • DARPP-32 is a dopamine and cAMP-regulated phosphoprotein that plays a critical role in the regulation of dopaminergic neurotransmission. The protein inhibits protein phosphatase I when it is phosphorylated on Thr^{34} and inhibits PKA when phosphorylated on Thr^{75}.

1 ea

Caspases

Item No.	Item Name	Applications	Species Reactivity/Specificity
13907	Caspase-1 Monoclonal Antibody (Clone 14F468)	IHC, WB	H, Mo
13906	Caspase-1 Polyclonal Antibody	IHC, WB	H
13908	Caspase-2 Monoclonal Antibody (Clone 18E809.3)	WB	H
13909	Caspase-3 Monoclonal Antibody (Clone 31A1067)	IHC, WB	H, Mo, R
160745	Caspase-3 (human) Polyclonal Antibody	WB, IHC	H, Mo, Bb
13911	Caspase-3 Monoclonal Antibody (Clone 31A893)	WB	H
13912	Caspase-7 Monoclonal Antibody (Clone 25B881.1)	IHC, WB	H, Mo, R
13914	Caspase-8 Monoclonal Antibody - biotin (Clone 90A992)	ELISA	H, RMk, Chimp
13913	Caspase-8 Monoclonal Antibody (Clone 90A992)	FC, IHC, WB	H, RMk, Chimp
13915	Caspase-9 (carboxy-terminal divergent) Polyclonal Antibody	WB	H, Mo, R
160790	Caspase-9 Polyclonal Antibody	WB	H
13916	Caspase-14 Monoclonal Antibody (Clone 70A1426)	FC, WB	H, Mo

β-Catenin Polyclonal Antibody 100029

Peptide affinity-purified IgG **Stability:** ≥6 months at 4°C
Summary: Antigen: human β-catenin amino acids 43-62 • Host: rabbit • Cross Reactivity: (+) human, mouse, rat, porcine, and bovine β-catenin • Application(s): IHC and WB • β-Catenin is a multifunctional protein known to be part of the Wnt pathway, playing essential roles in development and carcinogenesis. It can act as a regulator of the cell cycle and apoptosis in a variety of different cell systems.

500 µl

•Also Available: **β-Catenin Blocking Peptide** (300013)

β-Catenin (Phospho-Ser^{33,37}) Polyclonal Antibody 10009180

Anti-Phospho-Ser^{33,37} β-Catenin
Affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: phosphopeptide corresponding to amino acid residues surrounding phospho-Ser^{33,37} of human β-catenin • Host: rabbit • Cross Reactivity: (+) human β-catenin • Application(s): WB • β-Catenin is a central component of the cadherin cell adhesion complex and plays an essential role in neural development in the Wingless/Wnt signaling pathway. It is thought to be regulated by the sequential phosphorylation of Ser^{29}, Ser^{33}, Ser^{37}, and Thr^{41} by GSK3β. This hyperphosphorylation promotes the ubiquitylation and targeted destruction of β-catenin.

1 ea

DcR2 Polyclonal Antibody 160755

TRAIL-R4, TRUNDD
Affinity-purified IgG **Stability:** ≥1 year at 4°C
Summary: Antigen: human DcR2 precursor amino acids 249-263 • Host: rabbit • Cross Reactivity: (+) human DcR2 • Application(s): WB • DcR2 has an extracellular TRAIL-binding domain but lacks an intracellular death domain and does not induce apoptosis. Like DR4 and DR5, DcR2 transcript is widely expressed in normal human tissues. Overexpression of DcR2 attenuates TRAIL-induced apoptosis.

1 ea

ERK/MAPK (Phospho-Thr^{202}/Tyr^{204}) Polyclonal Antibody 10009179

Affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: phosphopeptide corresponding to amino acid residues surrounding phospho-Thr^{202} and phospho-Tyr^{204} of rat ERK/MAPK • Host: rabbit • Cross Reactivity: (+) human and rat ERK/MAPK • Application(s): WB • ERK/MAPK is an integral component of cellular signaling during mitogenesis and differentiation of mitotic cells and also is thought to play a key role in learning and memory. The activity of this kinase is regulated by dual phosphorylation at Thr^{202} and Tyr^{204}.

1 ea

FKBP52 Monoclonal Antibody (Clone Hi52C) 10011442

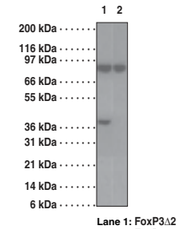
FK-506 Binding Protein 52
Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human FKBP52 • Host: mouse, clone Hi52C • Isotype: IgG_1 • Cross Reactivity: (+) canine, hamster, human, mouse, and rat FKBP52 • Application(s): IHC (paraffin-embedded sections), IP, and WB • FKBP52 is part of the mature glucocorticoid receptor heterocomplex. The N-terminal domain binds FK506 and has peptidyl-prolyl isomerase activity that converts prolyl peptide bonds within target proteins from *cis*- to *trans*- proline. The C-terminal domains contain the TRP repeats involved in protein-protein interactions with Hsp40.

25 µg
100 µg

FoxP3Δ2 (exon 2 deleted) Specific Monoclonal Antibody (Clone 16J4G6) 13744

Ammonium sulfate-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: peptide corresponding to the exon 2 deletion site • Host: mouse, clone 16J4G6 • Isotype: $IgM_κ$ • Cross Reactivity: (+) human FoxP3Δ2 • Application(s): WB • FoxP3 is a transcription factor that is a specific molecular marker essential for the development and function of Tregs.

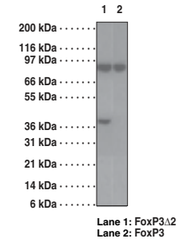
1 ea



FoxP3Δ2 (exon 2 deleted) Specific Monoclonal Antibody (Clone 16J4G6) (azide free) 13743

Ammonium sulfate-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: peptide corresponding to the exon 2 deletion site • Host: mouse, clone 16J4G6 • Isotype: $IgM_κ$ • Cross Reactivity: (+) human FoxP3Δ2 • Application(s): WB • FoxP3 is a transcription factor that is a specific molecular marker essential for the development and function of Tregs.

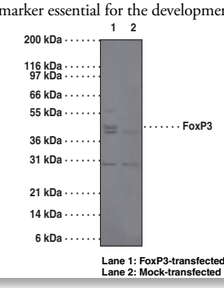
1 ea



FoxP3/Scurfin Polyclonal Antibody 13739

Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: peptide corresponding to the exon 2 deletion site • Host: rabbit • Cross Reactivity: (+) bovine, chicken, equine, human, porcine, rat, and Rhesus monkey FoxP3/Scurfin • Application(s): IHC and WB • FoxP3 is a transcription factor that is a specific molecular marker essential for the development and function of Tregs.

1 ea



GSK3β (Phospho-Ser^{9}) Polyclonal Antibody 10009374

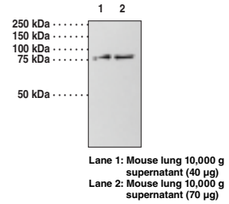
Anti-Phospho-Ser^{9} Glycogen Synthase Kinase 3β
Peptide affinity-purified antibody **Stability:** ≥1 year at -20°C
Summary: Antigen: phosphopeptide corresponding to amino acid residues surrounding phospho-Ser^{9} of GSK3β • Host: rabbit • Cross Reactivity: (+) rat GSK3β • Application(s): WB • GSK3 is a serine/threonine kinase that is involved in the regulation of many signaling pathways. GSK3β plays a key inhibitory role in both the insulin and Wnt signaling pathways.

1 ea

Guanylate Cyclase α subunit (soluble) Polyclonal Antibody 160895

sGC $α_1$ subunit
Affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human sGC $α_1$ subunit amino acids 418-436 • Host: rabbit • Cross Reactivity: (+) mouse, human, and bovine sGC $α_1$ subunit • Application(s): WB • Soluble guanylate cyclase is a heterodimeric enzyme, composed of α and β subunits, that synthesizes cGMP from GTP. The enzyme is activated by the binding of NO or carbon monoxide to the heme group of the enzyme.

500 µl

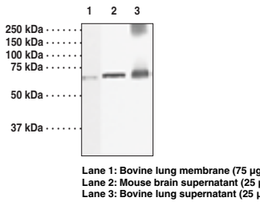


•Also Available: **Guanylate Cyclase α subunit (soluble) Blocking Peptide** (360895)

Guanylate Cyclase $β_1$ subunit (soluble) Polyclonal Antibody 160897

sGC $β_1$ subunit
Peptide affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: rat sGC $β_1$ subunit amino acids 188-207 • Host: rabbit • Cross Reactivity: (+) most mammalian species • Application(s): IHC and WB • Soluble guanylate cyclase is a heterodimeric enzyme, composed of α and β subunits, that synthesizes cGMP from GTP. The enzyme is activated by the binding of NO or carbon monoxide to the heme group of the enzyme.

500 µl



•Also Available: **Guanylate Cyclase $β_1$ subunit (soluble) Blocking Peptide** (360897)

HIF-1α Monoclonal Antibody (Clone H1α67) 10347

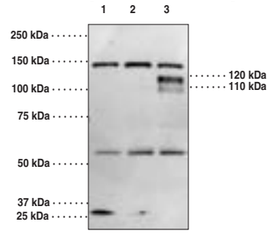
Hypoxia Inducible Factor-1α
Protein-A purified IgG_{2b} **Stability:** ≥1 year at -20°C
Summary: Antigen: human HIF-1α amino acids 432-528 • Host: mouse, clone H1α67 • Cross Reactivity: (+) ferret, human, mouse, and ovine HIF-1α • Application(s): IHC and WB • HIF-1α is a transcription factor that accumulates under low-oxygen conditions and helps to drive the production of stress-adaptive proteins.

1 ea

HIF-1α (C-Term) Polyclonal Antibody 10006421

Hypoxia Inducible Factor-1α
Peptide affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: HIF-1α C-terminal amino acids 809-826 • Host: rabbit • Cross Reactivity: (+) human, mouse, and simian HIF-1α • Application(s): (+) WB; (-) ICC and IP • HIF-1α is a transcription factor that accumulates under low-oxygen conditions. Following hypoxic stimulus and cytoplasmic accumulation, HIF-1α migrates to the nucleus where, with other transcription factors, it drives the production of stress-adaptive proteins. This response is essential for maintenance of normal oxidative physiology, however overexpression in cancer cells promotes tumor survival.

1 ea



Lane 1: Cos cell lysate (30 µg)
Lane 2: Cos cell lysate (40 µg)
Lane 3: $CoCl_2$ treated Cos cell lysate (30 µg)

•Also Available: **HIF-1α (C-Term) Blocking Peptide** (300003)

HIF-2α Polyclonal Antibody 13505

Hypoxia Inducible Factor-2α
Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human HIF-2α amino acids 426-443 • Host: rabbit • Cross Reactivity: (+) human HIF-2α • Application(s): WB • The hypoxia inducible factors (HIF-1α and HIF-2α) are transcription factors that directly respond to hypoxic stress. After exposure of normal and cancer cells to hypoxia, a rapid increase of HIF-1α and HIF-2α heterodimerization with the HIF-1α protein (ARNT) occurs, leading to increased transcription of HIF target genes.

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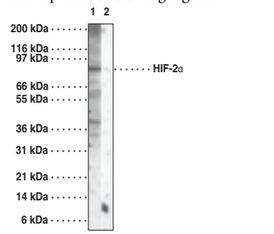

Lane 1: $CoCl_2$-Treated HeLa cell lysate
Lane 2: Untreated HeLa cell lysate

HMGB1 Monoclonal Antibody (Clone IMG19N12A1) 11514

High Mobility Group Protein B1, HMG1
Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: full-length recombinant human HMGB1 • Host: mouse, clone IMG19N12A1 • Isotype: $IgG_{2bκ}$ • Cross Reactivity: (+) human and mouse HMGB1 • Application(s): WB • HMGB1 is a necessary and sufficient mediator of inflammation during sterile and infection-associated responses. HMGB1 also act as DNA nuclear binding protein that has been shown to be an early trigger of sterile inflammation in animal models of trauma-hemorrhage *via* the activation of the TLR4 and RAGE.

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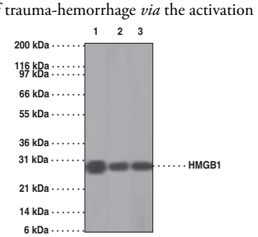
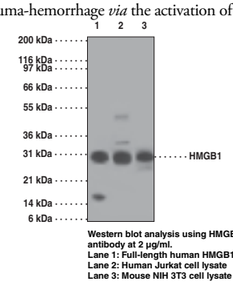


Western blot analysis using HMGB1 antibody at 2 µg/ml.
Lane 1: Full-length human HMGB1
Lane 2: Human HeLa cell lysate
Lane 3: Mouse NIH 3T3 cell lysate

HMGB1 Monoclonal Antibody (Clone IMG19N10B7) 11512

High Mobility Group Protein B1, HMG1
Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: full-length human HMGB1 • Host: mouse, clone IMG19N10B7 • Isotype: $IgG_{2bκ}$ • Cross Reactivity: (+) human and mouse HMGB1 • Application(s): FC, IHC (paraffin), and WB • HMGB1 is a necessary and sufficient mediator of inflammation during sterile and infection-associated responses. HMGB1 also act as DNA nuclear binding protein that has been shown to be an early trigger of sterile inflammation in animal models of trauma-hemorrhage *via* the activation of TLR4 and RAGE.

1 ea

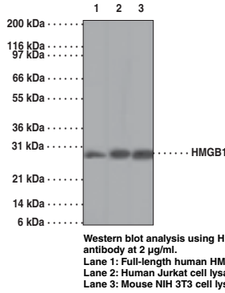


Western blot analysis using HMGB1 antibody at 2 µg/ml.
Lane 1: Full-length human HMGB1
Lane 2: Human Jurkat cell lysate
Lane 3: Mouse NIH 3T3 cell lysate

HMGB1 Monoclonal Antibody (Clone IMG19N15F4) 11513

High Mobility Group Protein B1, HMG1
Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: full-length recombinant human HMGB1 • Host: mouse, clone IMG19N15F4 • Isotype: IgG_{1k} • Cross Reactivity: (+) human and mouse HMGB1 • Applications: FC, IHC (paraffin), and WB • HMGB1 is a necessary and sufficient mediator of inflammation during sterile and infection-associated responses. HMGB1 also act as DNA nuclear binding protein that has been shown to be an early trigger of sterile inflammation in animal models of trauma-hemorrhage *via* the activation of TLR4 and RAGE.

1 ea

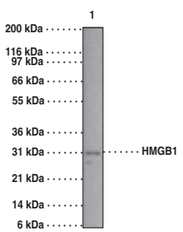


Western blot analysis using HMGB1 antibody at 2 µg/ml.
Lane 1: Full-length human HMGB1
Lane 2: Human Jurkat cell lysate
Lane 3: Mouse NIH 3T3 cell lysate

HMGB1 Polyclonal Antibody (aa 25-75) 11516

High Mobility Group Protein B1, HMG1
Protein A-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: portion of amino acids 25-75 of human HMGB1 • Host: rabbit • Cross Reactivity: (+) human, chicken, mouse, New World monkey, and rat HMGB1 • Application(s): WB • HMGB1 is a necessary and sufficient mediator of inflammation during sterile and infection-associated responses. HMGB1 also act as DNA nuclear binding protein that has been shown to be an early trigger of sterile inflammation in animal models of trauma-hemorrhage *via* the activation of TLR4 and RAGE.

1 ea

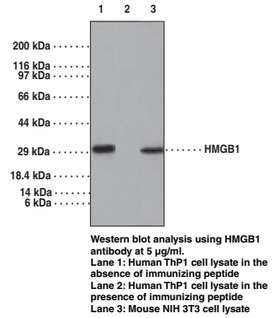


Western blot analysis using HMGB1 antibody at 5 µg/ml.
Lane 1: Mouse NIH 3T3 cell lysate

HMGB1 Polyclonal Antibody (aa 100-150) 11515

High Mobility Group Protein B1, HMG1
Protein A-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: portion of amino acids 100-150 of human HMGB1 • Host: rabbit • Cross Reactivity: (+) human, chicken, bovine, mouse, New World monkey, and rat HMGB1 • Application(s): FC, IHC (paraffin), WB • HMGB1 is a necessary and sufficient mediator of inflammation during sterile and infection-associated responses. HMGB1 also act as DNA nuclear binding protein that has been shown to be an early trigger of sterile inflammation in animal models of trauma-hemorrhage *via* the activation of TLR4 and RAGE.

1 ea

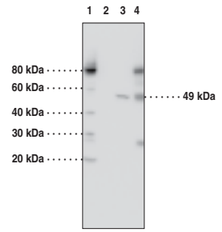


Western blot analysis using HMGB1 antibody at 5 µg/ml.
Lane 1: Human ThP1 cell lysate in the absence of immunizing peptide
Lane 2: Human ThP1 cell lysate in the presence of immunizing peptide
Lane 3: Mouse NIH 3T3 cell lysate

IP6K2 Monoclonal Antibody (Clone 4F10) 10239

IHPK2, Inositol Hexakisphosphate Kinase 2
Protein A-purified IgG **Stability:** ≥2 years at -20°C
Summary: Antigen: human IP6K2 • Host: mouse, clone 4F10 • Isotype: $IgG_{2bκ}$ • Cross Reactivity: (+) human and mouse IP6K2 • Application(s): ICC and WB • IP6K2 is a cytoplasmic kinase that catalyzes the conversion of IP6 to diphosphoinositol pentakisphosphate in the presence of ATP. IP6K2 functions as a proapoptotic protein kinase and binds to tumor necrosis factor receptor-associated factor 2 and inhibits NF-κB signaling.

1 ea

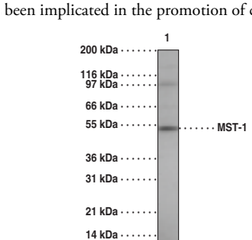


Lane 1: MW Standard
Lane 2: IP6K2 control lysate (10 µg)
Lane 3: IP6K2 over expressed lysate (10 µg)
Lane 4: Mouse small intestine supernatant (30 µg)

Mammalian STE-20-Like Kinase 1 Polyclonal Antibody 13776

KRS2, MST-1, STK4
Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human MST-1 amino acids 372-390 • Host: rabbit • Cross Reactivity: (+) human MST-1 • Application(s): WB • MST-1 is a serine/threonine kinase that has been implicated in the promotion of chromatin condensation.

1 ea



Lane 1: Jurkat cell lysate

MEK1 (Phospho-Thr^{292}) Polyclonal Antibody 10009518

MAP Kinase Kinase 1, MAPKK1
Affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: phosphopeptide corresponding to amino acid residues surrounding phospho-Thr^{292} of human MEK1 • Host: rabbit • Cross Reactivity: (+) human and rat MEK1; expected to react with bovine, canine, chicken, mouse, non-human primates, and *Xenopus* MEK1 • Application(s): WB • MEK1 is an integral component of the MAPK cascade that regulates cell growth and differentiation. MEK1 is phosphorylated by MAPK on Thr^{292} and Thr^{386}.

1 ea

MEK1 (Phospho-Thr^{386}) Polyclonal Antibody 10009517

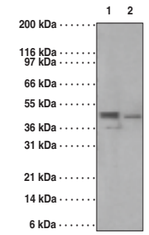
MAP Kinase Kinase 1, MAPKK1
Affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: phosphopeptide corresponding to amino acid residues surrounding phospho-Thr^{386} of human MEK1 • Host: rabbit MEK1 • Cross Reactivity: (+) rat MEK1 • Application(s): WB • MEK1 is an integral component of the MAPK cascade that regulates cell growth and differentiation. MEK1 is phosphorylated by MAPK on Thr^{292} and Thr^{386}.

1 ea

MEK1/2 Polyclonal Antibody 13846

MAP Kinase Kinase 1/2, MAPKK1/2
Peptide affinity-purified IgG **Stability:** ≥6 months at -20°C
Summary: Antigen: synthetic peptide corresponding to a portion of human MEK1 amino acids 200-250 • Host: rabbit • Cross Reactivity: (+) chicken, chimpanzee, ovine, canine, *Drosophila*, human, mouse, and rat MEK1/2 • Application(s): WB • MEK1 and MEK2 are integral components of the MAPK cascade that regulates cell growth and differentiation and plays a key role in synaptic plasticity in the brain. MEK1/2 is activated *via* phosphorylation of Ser^{218} and Ser^{222}. When activated MEK1/2 acts as a dual specificity kinase phosphorylating both a threonine and a tyrosine residue on ERK.

1 ea



A375 whole cell lysate showing:
Lane 1: Phosphorylated MEK1/2 (upper band) and unphosphorylated MEK1/2 (lower band)
Lane 2: Nonphosphorylated MEK1/2

MEK1/2 (Phospho-Ser^{218,222}) Polyclonal Antibody 10009178

MAP Kinase Kinase 1/2, MAPKK1/2
Affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: phosphopeptide corresponding to amino acid residues surrounding phospho-Ser^{218,222} of human MEK1/2 • Host: rabbit • Cross Reactivity: (+) NIH 3T3 cells • Application(s): WB • MEK1 is an integral component of the MAPK cascade that regulates cell growth and differentiation.

1 ea

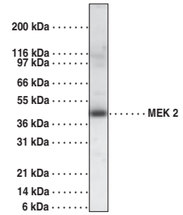
MEK2 Polyclonal Antibody 13847

Dual Specificity MAP Kinase Kinase 2, MAP Kinase/ERK Kinase 2, MAP Kinase Kinase 2, MAPKK2

Protein affinity-purified IgG **Stability:** ≥6 months at -20°C

Summary: Antigen: peptide from human MEK2 • Host: rabbit • Cross Reactivity: (+) human MEK2 • Application(s): WB • Human MEK2 is activated through phosphorylation of its serine residues at positions 222 and 226 by a variety of cytokines and growth factors. It is responsible for the phosphorylation/activation of MAP kinases and ERKs, and is an essential component in the transduction of mitogenic signals.

1 ea



Lane 1: 293 cell lysate

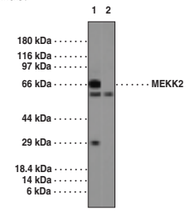
MEKK2 Polyclonal Antibody 13848

Dual Specificity MAP Kinase Kinase Kinase 2, MAP3K2, MAPKKK2

Protein G-purified IgG **Stability:** ≥6 months at -20°C

Summary: Antigen: peptide within the region of human MEKK2 amino acids 1-50 • Host: rabbit • Cross Reactivity: (+) human MEKK2 • Application(s): IHC (paraffin embedded-sections) and WB • MEKK2 directly phosphorylates and activates IκB kinases. It regulates T cell function, controls cytokine gene expression in mast cells, mediates EGFR and fibroblast growth factor-2 receptor signals, and plays a role in rheumatoid arthritis.

1 ea



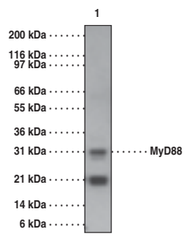
Lane 1: Human liver cell lysate (absence of immunizing peptide)
Lane 2: Human liver cell lysate (presence of immunizing peptide)

MyD88 Polyclonal Antibody 13746

Protein G-purified IgG **Stability:** ≥1 year at -20°C

Summary: Antigen: human MyD88 amino acid 233-248 • Host: rabbit • Cross Reactivity: (+) human, mouse, and rat MyD88 • Application(s): WB • MEK1 and MEK2 are integral components of the MAPK cascade that regulates cell growth and differentiation and plays a key role in synaptic plasticity in the brain. MEK1/2 is activated *via* phosphorylation of Ser^{218} and Ser^{222}. When activated MEK1/2 acts as a dual specificity kinase phosphorylating both a threonine and a tyrosine residue on ERK.

1 ea



Lane 1: Human spleen cell lysate

Nod2 Monoclonal Antibody (Clone 2D9) 10004942

Protein A-purified $IgG_{1κ}$ **Stability:** ≥1 year at 4°C

Summary: Antigen: recombinant human Nod2 amino acids 28-301 • Host: mouse, clone 2D9 • Cross Reactivity: (+) human Nod2 • Application(s): IHC and WB • Nod2 is a member of the apoptosis regulating protein family that has CARDs and also includes Apaf-1 and Nod1. Nod1 and Nod2 act as intracellular receptors for bacterial LPS, activate NF-κB, and contribute to inflammatory bowel disease.

1 ea

Lane 1: Sham transfected 293T lysate (10 µg)
Lane 2: Nod2 transfected 293T lysate (10 µg)

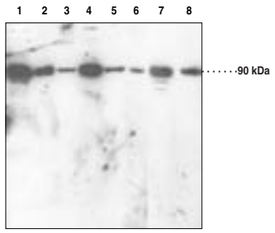
Nrf2 (C-Term) Polyclonal Antibody 10214

GABPA, HEBP1, Nuclear Factor Erythroid 2-related factor 2

Affinity-purified IgG **Stability:** ≥2 years at -20°C

Summary: Antigen: human Nrf2 C-terminal amino acids 579-592 • Host: rabbit • Cross Reactivity: (+) human, mouse, and rat Nrf2 • Application(s): FC, ICC, and WB • This C-terminal Nrf2 polyclonal antibody preferentially detects poly-ubiquitination Nrf2 at 90 kDa. Nrf2 forms a heterodimer with a small Maf protein and binds to the ARE in the upstream promoter region of many antioxidative genes. Under normal, unstressed conditions, Nrf2 is sequestered in the cytoplasm where it is bound by Keap1 and cullin 3. Certain stressors disrupt Keap 1 binding and prevent ubiquitination, leading to subsequent translocation into the nucleus.

1 ea



Lane 1: HeLa cell lysate (50 µg)
Lane 2: Mouse small intestine (50 µg)
Lane 3: Mouse heart (50 µg)
Lane 4: HepG2 cell lysate (50 µg)
Lane 5: Rat liver (50 µg)
Lane 6: Rat liver sample (50 µg)
Lane 7: Mouse liver (50 µg)
Lane 8: Mouse skeletal muscle (50 µg)

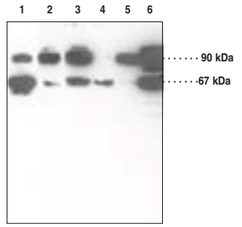
NF-κB Signaling Pathway

Item No.	Item Name	Applications	Species Reactivity/Specificity
13925	IκBα (cleavage specific) Monoclonal Antibody (Clone 5D1623)	WB	H
13918	IκBα Monoclonal Antibody (Clone 6A920)	FC, IHC, IP, WB	H, Mo
13922	IκBα Monoclonal Antibody - biotin (Clone 6A920)	ELISA	H, Mo
13923	IκBα (Phospho-$Ser^{32/36}$) Monoclonal Antibody (Clone 39A1413)	IP, WB	Bo, C, H, Mo, P, R
13924	IκBα (Phospho-$Ser^{32/36}$) Monoclonal Antibody - biotin (Clone 39A1413)	ELISA	Bo, C, H, Mo, P, R
13921	IκBα Polyclonal Antibody	WB	Mo; (-) H IκBα
13919	IκBα Polyclonal Antibody (aa 34-48)	WB	H
13926	IκBζ Polyclonal Antibody	WB	Mo
13927	IKKα Monoclonal Antibody (Clone 14A231)	FC, IHC, IP, WB	H, Mk, Mo
13929	IKKε Monoclonal Antibody (Clone 72B587)	FC, WB	H, Mo, R
13928	IKKε Polyclonal Antibody	WB	H
13930	IKKγ Monoclonal Antibody (Clone 46B844)	FC, WB	H, Mk, Mo
13931	IKKγ Monoclonal Antibody (Clone 72C627)	WB	H, Mo
13843	IRAK-1 Polyclonal Antibody	IP, WB	H, Mo; (-) IRAK-2
13844	IRAK-2 Polyclonal Antibody	WB	H, Mo
13845	IRAK-4 Polyclonal Antibody	IP, WB	H, Mo
11511	JNK2 Polyclonal Antibody	WB	H
13755	NF-κB (p50) Monoclonal Antibody (Clone 2J10D7)	IHC, WB	H
13754	NF-κB (p50) Polyclonal Antibody	WB	Chimp, H, RMk
13752	NF-κB (p65) Monoclonal Antibody (Clone 112A1021)	FC, IHC, WB	H, Mo, R
13756	NF-κB (p65) Monoclonal Antibody-biotin (Clone 112A1021)	ELISA	H, Mo, R
13751	NF-κB (p65) NLS Polyclonal Antibody	ICC, WB	B, Chimp, Gr, E, H, Mk, Mo
13757	NF-κB (p65) Polyclonal Antibody (aa 2-17)	WB	Chimp, H, Mk
13753	NF-κB (p65) Polyclonal Antibody (aa 538-546)	WB	H, Mo, R
10846	STAT1α/β Polyclonal Antibody	WB	Chimp, C, H, Mo, Sh
10847	STAT2 Polyclonal Antibody	WB	H
10861	STAT3 (Phospho-Tyr^{705}) Polyclonal Antibody	WB	Chimp, C, H, Mo, RMk
10856	STAT5β Polyclonal Antibody	WB	Bo, Ch, NWMk, Mo, R
10931	STAT6 Polyclonal Antibody	ICC, WB	H, Mo, R
10855	TRAF2 Monoclonal Antibody (Clone 33A1293)	WB	H
10873	TRAF5 Monoclonal Antibody (Clone 55A219)	WB	H, Mo
10874	TRAF6 Polyclonal Antibody	WB	H, Mo
10894	TRAF6BP Polyclonal Antibody	WB	H
160750	TRAIL Polyclonal Antibody	WB	H, Mo (expected)

Nrf2 (N-Term) Polyclonal Antibody 14114

GABPA, HEBP1, Nuclear Factor Erythroid 2-related factor 2
Affinity-purified IgG **Stability:** ≥2 years at -20°C
Summary: Antigen: human Nrf2 C-terminal amino acids 18-29 • Host: rabbit • Cross Reactivity: (+) human, mouse, and rat Nrf2 • Application(s): FC, ICC, and WB • This N-terminal Nrf2 polyclonal antibody detects both poly-ubiquitination Nrf2 at 90 kDa and native Nrf2 at 67 kDa. Nrf2 forms a heterodimer with a small Maf protein and binds to the ARE in the upstream promoter region of many antioxidative genes. Under normal, unstressed conditions, Nrf2 is sequestered in the cytoplasm where it is bound by Keap1 and cullin 3. Certain stressors disrupt Keap 1 binding and prevent ubiquitination, leading to subsequent translocation into the nucleus.

1 ea

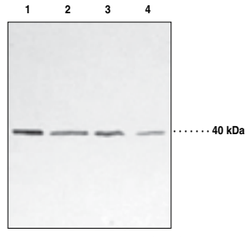


Lane 1: HeLa cell lysate (50 µg)
Lane 2: Mouse heart (50 µg)
Lane 3: Mouse liver (50 µg)
Lane 4: Mouse kidney (50 µg)
Lane 5: A549 cell lysate (50 µg)
Lane 6: Mouse skeletal muscle (50 µg)

p38 MAPK Monoclonal Antibody (Clone 9F12) 10011301

p38 MAPKα, p38 Mitogen-activated Protein Kinase
IgG_1 **Stability:** ≥1 year at -20°C
Summary: Antigen: human full length p38 MAPK • Host: mouse, clone 9F12 • Cross Reactivity: (+) human, mouse, and rat p38 MAPK • Application(s): FC, ICC, and WB • p38 MAPK is a member of the serine-threonine MAPK family that triggers many cellular processes including cell cycle, development, and apoptosis.

1 ea



Lane 1: Human platelet lysate (25 µg)
Lane 2: Jurkat cell lysate (25 µg)
Lane 3: RAW 264.7 cell lysate (50 µg)
Lane 4: Rat heart supernatant (25 µg)

p38 MAPK (Phospho-Thr^{180}/Tyr^{182}) Polyclonal Antibody 10009177

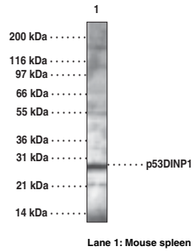
Anti-Phospho-Thr^{180}/Tyr^{182} p38 MAPK
Affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: phosphopeptide corresponding to amino acid residues surrounding phospho-Thr^{180} and phospho-Tyr^{182} of rat p38 MAPK • Host: rabbit • Cross Reactivity: (+) human p38 MAPK • Application(s): WB • p38 MAPK is activated by both inflammatory cytokines and by stress. It is thought to be particularly important in diseases like asthma and autoimmunity but it also plays important roles in the stress response of the nervous system. Like the other MAPKs, p38 is activated by a dual specificity kinase that phosphorylates Thr^{180} and Tyr^{182}.

1 ea

p53DINP1 Polyclonal Antibody 10993

SIP, TP53INP1
Antibody **Stability:** ≥1 year at -20°C
Summary: Antigen: synthetic peptides from human p53DINP1 • Host: rabbit • Cross Reactivity: (+) human, mouse, and rat p53DINP1 • Application(s): WB • p53DINP1 is a novel p53 inducible gene that may regulate p53-dependent apoptosis through phosphorylation at Ser^{46} and induction of p53AIP1.

1 ea

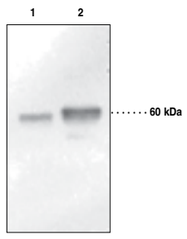


Lane 1: Mouse spleen

p53 Monoclonal Antibody (Clone BP53-12) 10004806

Purified IgG_{2a} **Stability:** ≥1 year at 4°C
Summary: Epitope: binds to N-terminal amino acids 16-25 of wild-type and mutant p53 • Host: mouse, clone BP53-12 • Isotype: IgG_{2a} • Cross Reactivity: (+) human p53 • Application(s): FC, ICC, IHC (paraffin-embedded sections), and WB; this antibody does not work with frozen sections • Cellular p53, often called the 'guardian of the genome,' is a transcription factor that is activated in response to cellular stress (DNA damage, hypoxia, heat shock, etc.) and acts to prevent further proliferation of the stressed cell by induction of cell cycle arrest or apoptotic mediators.

1 ea



Lane 1: Human lung cancer lysate (30 µg)
Lane 2: Resveratrol-treated human lung cancer cell lysate (30 µg)

p53 (Phospho-Ser^{392}) Polyclonal Antibody 10004807

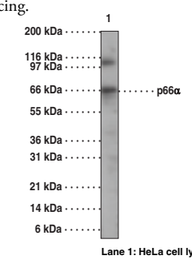
Affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: amino acids around phospho-Ser^{392} • Host: rabbit • Application(s): WB • Nearly 50% of human tumors have mutated or non-functional p53. p53 amino acid residues can be modified by phosphorylation and acetylation. *In vivo* phosphorylation of p53 residues alters signal transduction events that warrant further investigation.

1 ea

p66α Polyclonal Antibody 13785

GATA Zinc Finger Domain-Containing Protein 2A, Transcriptional Repressor p66α
IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: mouse p66α amino acids 572-585 • Host: rabbit • Cross Reactivity: (+) human, mouse, and rat p66α • Application(s): WB • p66 is one of the components of the MeCP1 complex, an HDAC core complex involved in methylated DNA silencing.

1 ea

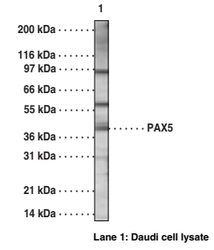


Lane 1: HeLa cell lysate

PAX5 Polyclonal Antibody 10992

BSAP
Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human PAX5 amino acids 1-15 • Host: rabbit • Cross Reactivity: (+) human and mouse PAX5 • Application(s): WB • Pax5 is an essential transcription factor and a critical regulator of B cell development. It is up-regulated by the IL-7 phosphorylated STAT5.

1 ea

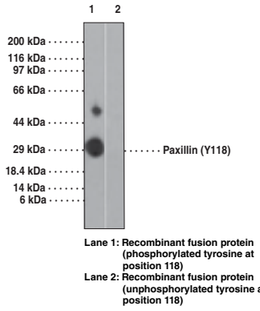


Lane 1: Daudi cell lysate

Paxillin (Phospho-Tyr^{118}) Polyclonal Antibody 10994

Antigen affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: portion of human Paxillin protein containing a phosphorylated tyrosine residue at position 118 • Host: rabbit • Cross Reactivity: (+) human, chicken, chimpanzee, dog, mouse, rat, and zebrafish Paxillin; predicted to react with *Xenopus* Paxillin • Application(s): WB • Paxillin is a protein with four LIM domains, a proline-rich domain containing a consensus SH3-binding site, and three potential SH2-binding sites. It acts as an ERK-regulated scaffold that coordinates FAK and Rac activation in epithelial morphogenesis. Phosphorylation of Paxillin by JNK is known to regulate cell migration.

1 ea

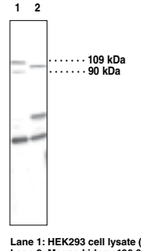


Lane 1: Recombinant fusion protein (phosphorylated tyrosine at position 118)
Lane 2: Recombinant fusion protein (unphosphorylated tyrosine at position 118)

PGC-1 Polyclonal Antibody 101707

Peroxisome Proliferator-activated Receptor γ Coactivator 1, PPARγ Coactivator 1
IgG **Stability:** ≥2 years at -20°C
Summary: Antigen: human PGC-1α amino acids 75-90 • Host: rabbit • Cross Reactivity: (+) human, mouse, and rat PGC-1α and PGC-1β • Application(s): IHC (paraffin-embedded sections) and WB • Three PGC-1 isoforms have been characterized - PGC-1α, -1β, and -1-related coactivator. PGC-1α and PGC-1β are inducible transcriptional coactivators for certain nuclear receptors and play a key role in energy metabolism, hepatic gluconeogenesis, and cholesterol homoeostasis. Changes in PGC-1 levels may play a role in metabolic disorders such as type II diabetes and obesity.

1 ea



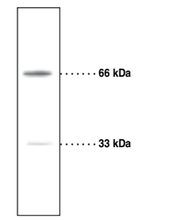
Lane 1: HEK293 cell lysate (40 µg)
Lane 2: Mouse kidney 100,000 x g pellet resuspension (40 µg)

•Also Available: **PGC-1 Blocking Peptide** (301707)

PINK1 Polyclonal Antibody 10006283

BRPK, PARK6, PTEN Induced Putative Kinase 1
Peptide affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human PINK1 amino acids 484-504 • Host: rabbit • Cross Reactivity: (+) human, mouse, and rat PINK1 • Application(s): IHC (paraffin-embedded sections) and WB • PINK1 was first identified when studying the tumor-suppressive function of the PTEN signaling pathway and is thus believed to be involved in human cancer pathology.

500 µl



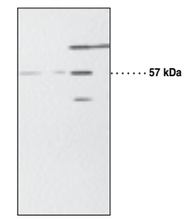
Lane 1: Mouse liver 100,000 x g pellet (30 µg)

•Also Available: **PINK1 Blocking Peptide** (10006284)

PPARα Polyclonal Antibody 101710

Peroxisome Proliferator-activated Receptor α
Peptide affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human, mouse, and rat PPARα amino acids 22-36 • Host: rabbit • Cross Reactivity: (+) human, mouse, rat, ovine, and porcine PPARα; (-) PPARγ • Application(s): WB • PPARα is a ligand-activated transcription factor involved in the regulation of lipid homeostasis

1 ea



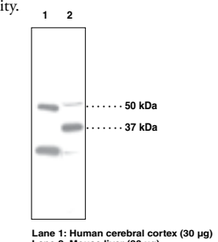
Lane 1: Baboon myometrium (100 µg)
Lane 2: Baboon myometrium (50 µg)
Lane 3: K-562 cell lysate (75 µg)

•Also Available: **PPARα Blocking Peptide** (301710)

PPARδ Polyclonal Antibody 101720

FAAR, NUC1, Nuclear Hormone Receptor 1, Peroxisome Proliferator-activated Receptor δ, PPARβ
Peptide affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human PPARδ amino acids 39-54 • Host: rabbit • Cross Reactivity: (+) human, mouse, ovine, porcine, and rat PPARδ • Application(s): ICC, IHC, and WB • PPARδ is ubiquitously expressed but is particularly abundant in tissues such as liver, intestine, kidney, abdominal adipose, and skeletal muscle, all of which are involved in lipid metabolism. PPARδ is a mediator of diverse physiological functions including lipid and cholesterol homeostasis, embryo implantation, cancer development, and obesity.

1 ea



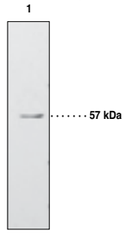
Lane 1: Human cerebral cortex (30 µg)
Lane 2: Mouse liver (30 µg)

•Also Available: **PPARδ Blocking Peptide** (10006247)

PPARγ Polyclonal Antibody 101700

Peroxisome Proliferator-activated Receptor γ
Peptide affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human PPARγ1 amino acids 82-101 (amino acids 110-129 of PPARγ2) • Host: rabbit • Cross Reactivity: (+) human and mouse PPARγ1 and PPARγ2 • Application(s): WB • PPARγ is a ligand-activated transcription factor involved in the regulation of lipid homeostasis and may function as a master regulator of adipogenesis.

500 µl



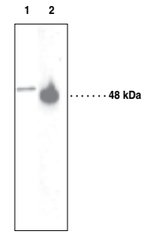
Lane 1: Rat adipose homogenate (30 µg)

•Also Available: **PPARγ Blocking Peptide** (301700)

PTEN Polyclonal Antibody 10005059

MMAC1, Phosphatase and Tensin Homolog on Chromosome 10, Phosphoinositide 3-phosphatase, TEP1
Peptide affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human PTEN amino acids 254-270 • Host: rabbit • Cross Reactivity: (+) human, mouse, chimpanzee, canine, and rat PTEN protein • Application(s): IHC (paraffin-embedded sections) and WB • PTEN dephosphorylates proteins and lipids such as Akt and PIP_3 and therefore functions as a key regulatory enzyme in a central signal transduction pathway. PTEN is considered a tumor suppressor as loss-of-function mutations in PTEN often result in human cancers including melanoma and prostate carcinoma.

500 µl



Lane 1: A431 cell lysate (50 µg)
Lane 2: Rat brain (30 µg)

•Also Available: **PTEN Blocking Peptide** (10007073)

Raf-1 (Phospho-Ser^{301}) Polyclonal Antibody 10009504

Affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: phosphopeptide corresponding to amino acid residues surrounding phospho-Ser^{301} of rat Raf-1 • Host: rabbit • Cross Reactivity: (+) rat Raf-1; expected to react with bovine, canine, chicken, human, mouse, non-human primate, and *Xenopus* Raf-1 • Application(s): WB • Studies have shown that phosphorylation is required for Raf-1 activation. Phosphorylation also down-regulates Raf with two sites participating: Ser^{301} and Ser^{642}.

1 ea

Raf-1 (Phospho-Ser^{642}) Polyclonal Antibody 10009505

Affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: phosphopeptide corresponding to amino acid residues surrounding phospho-Ser^{642} of rat Raf-1 • Host: rabbit • Cross Reactivity: (+) rat Raf-1; expected to react with bovine, canine, chicken, human, mouse, non-human primate, and *Xenopus* Raf-1 • Application(s): WB • Members of the Raf serine/threonine kinase family function to relay signals from activated Ras to the downstream protein kinases MEK and ERK, which are critical for cellular proliferation, differentiation, survival, and oncogenic transformation. Raf-1 activity is regulated by phophorylation of Ser^{301} and Ser^{642}.

1 ea

Ribosomal S6 Kinase 2 Polyclonal Antibody 10009411

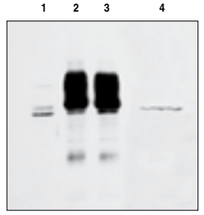
RSK2
Peptide affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: peptide corresponding to amino acid residues from the C-terminal region of rat RSK2 • Host: rabbit • Cross Reactivity: (+) rat RSK2 • Application(s): WB • RSKs 1-4 are downstream members of the ERK/MAPK cascade. Recent work suggests that RSK2 exerts a tonic regulation on G protein-coupled signaling.

1 ea

RICK Polyclonal Antibody 160785

CARDIAK, RIP2, Ripk2
Affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human RICK amino acids 11-30 • Host: rabbit • Application(s): WB • Overexpression of RICK promotes the activation of caspase-8 and Fas-induced apoptosis. RICK represents a novel kinase that regulates Fas-induced apoptosis.

500 µl



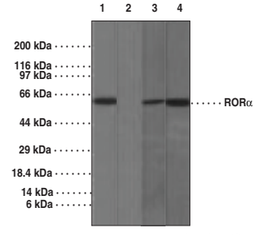
Lane 1: 293 T cell lysate
Lane 2: RICK transfected 293 T cell lysate
Lane 3: RICK transfected 293 T cell lysate
Lane 4: HeLa cell lysate

•Also Available: **RICK Blocking Peptide** (301785)

RORα Polyclonal Antibody (aa 80-120) 11077

NR1F1, RAR-Related Orphan Receptor A, Retinoid-Related Orphan Receptor α, RZR-α
Antigen affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: portion of amino acids 80-120 of human RORα • Host: rabbit • Cross Reactivity: (+) human, bovine, canine, chicken, chimpanzee, and mouse RORα; predicted to react with equine, opossum, sheep, and zebrafish RORα • Application(s): WB • RORα is a receptor for retinoic acid belonging to the NR1 subfamily of nuclear hormone receptors with a nuclear receptor DNA binding domain. RORα binds either as a monomer or as a homodimer to the retinoic acid response element and thus regulates gene expression and also controls cell function.

1 ea

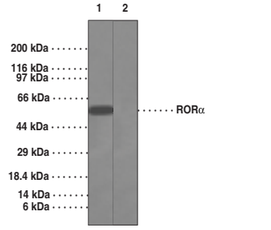


Western blot analysis using RORα antibody.
Lane 1: Human skeletal muscle lysate (absence of immunizing peptide) (0.25 µg/ml)
Lane 2: Human skeletal muscle lysate (presence of immunizing peptide) (0.25 µg/ml)
Lane 3: Mouse skeletal muscle lysate (0.01 µg/ml)
Lane 4: Rat skeletal muscle lysate (0.01 µg/ml)

RORα Polyclonal Antibody (aa 220-270) 11078

NR1F1, RAR-Related Orphan Receptor A, Retinoid-Related Orphan Receptor α, RZR-α
Antigen affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: portion of amino acids 220-270 of human RORα • Host: rabbit • Cross Reactivity: (+) human, bovine, canine, chicken, chimpanzee, equine, and New World monkey RORα; (-) mouse RORα; predicted to react with canine and *Xenopus* RORα • Application: WB • RORα is a receptor for retinoic acid belonging to the NR1 subfamily of nuclear hormone receptors with a nuclear receptor DNA binding domain. RORα binds either as a monomer or as a homodimer to the retinoic acid response element and thus regulates gene expression and also controls cell function.

1 ea

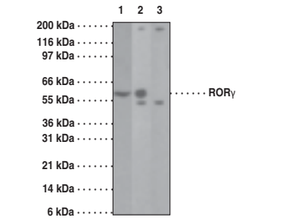


Lane 1: Human skeletal muscle lysate (absence of immunizing peptide) (0.025 µg/ml)
Lane 2: Human skeletal muscle lysate (presence of immunizing peptide) (0.025 µg/ml)

RORγ Monoclonal Antibody (Clone 4G419) 11002

NR1F3, RAR-Related Orphan Receptor C, Retinoid-Related Orphan Receptor γ
Peptide affinity-purified IgG **Stability:** ≥6 months at -20°C
Summary: Antigen: peptide within the region of amino acids 1-50 of human RORγ • Host: mouse • Cross Reactivity: (+) chimpanzee, human, and mouse RORγ • Application(s): FC and WB • RORγ is a DNA-binding transcription factor belonging to the ROR/RZR orphan nuclear receptor subfamily. RORγ inhibits the expression of Fas ligand and IL-2 and directs the differentiation program of proinflammatory IL-17$^+$ T helper cells.

1 ea

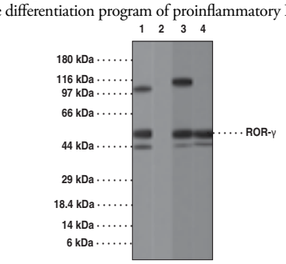


Lane 1: Human thymus lysate
Lane 2: Transfected 293 cell lysate
Lane 3: Untransfected 293 cell lysate

RORγ Polyclonal Antibody 11003

NR1F3, RAR-Related Orphan Receptor C, Retinoid-Related Orphan Receptor γ
Peptide affinity-purified IgG **Stability:** ≥6 months at -20°C
Summary: Antigen: peptide within the region of amino acids 1-50 of human RORγ • Host: rabbit • Cross Reactivity: (+) chimpanzee and human RORγ • Application(s): IHC and WB • RORγ is a DNA-binding transcription factor belonging to the ROR/RZR orphan nuclear receptor subfamily. ROR-γ inhibits the expression of Fas ligand and IL-2 and directs the differentiation program of proinflammatory IL-17$^+$ T helper cells.

1 ea

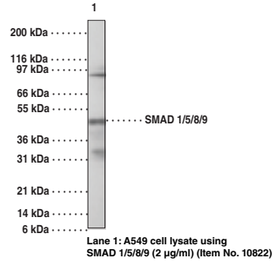


Lane 1: Jurkat cell lysate (absence of immunizing peptide)
Lane 2: Jurkat cell lysate (presence of immunizing peptide)
Lane 3: 3T3 cell lysate
Lane 4: RAW cell lysate

SMAD1/5/8/9 Polyclonal Antibody 10822

Antibody **Stability:** ≥6 months at -20°C
Summary: Antigen: human SMAD1 amino acids 19-33 and amino acids 315-330 • Host: rabbit • Cross Reactivity: (+) human, mouse, and rat SMAD1/5/8/9 • Application(s): WB • SMADs can be divided into receptor-regulated SMADs (R-SMADs: SMAD1/2/5/8/9), common-mediator SMAD (co-SMAD: SMAD4), and inhibitory SMADs (I-SMADs: SMAD6/7). SMAD1/5/8/9 have high degrees of homology and antibodies are available that recognize sequences common to all of them.

100 µg

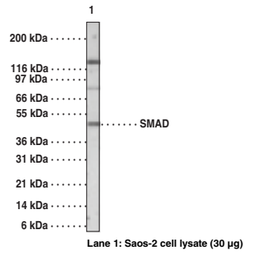


Lane 1: A549 cell lysate using SMAD 1/5/8/9 (2 µg/ml) (Item No. 10822)

SMAD1/5/8/9 Polyclonal Antiserum 10821

Polyclonal antiserum **Stability:** ≥6 months at -20°C
Summary: Antigen: human SMAD1 amino acids 19-33 and amino acids 315-329 • Host: rabbit • Cross Reactivity: (+) human, mouse, and rat SMAD1/5/8/9 • Application(s): WB • SMADs can be divided into receptor-regulated SMADs (R-SMADs: SMAD1/2/5/8/9), common-mediator SMAD (co-SMAD: SMAD4), and inhibitory SMADs (I-SMADs: SMAD6/7). SMAD1/5/8/9 have high degrees of homology and antibodies are available that recognize sequences common to all of them.

1 ea

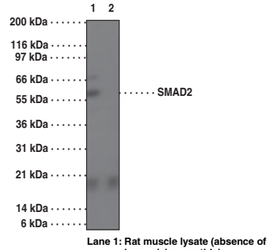


Lane 1: Saos-2 cell lysate (30 µg)

SMAD2 Polyclonal Antibody 10823

Protein G-purified IgG **Stability:** ≥6 months at -20°C
Summary: Antigen: human SMAD2 amino acids 234-249 • Host: rabbit • Cross Reactivity: (+) bovine, canine, chicken, chimpanzee, human, mouse, and rat SMAD2 • Application(s): IHC and WB • SMAD2 is an intracellular protein that associates with SMAD4 for translocation to the nucleus. It acts as an intracellular mediator of the TGFβ family of cytokines and activin type 1 receptor, regulating multiple cellular processes like cell growth, proliferation, differentiation, and apoptosis and also cooperating with transcription factors to regulate expression of defined genes.

100 µg



Lane 1: Rat muscle lysate (absence of immunizing peptide)
Lane 2: Rat muscle lysate (presence of immunizing peptide)

Oxygen Signaling Through HIF

by [Thomas G. Brock, Ph.D.]

The normal air that you breathe is 21% oxygen, for a partial pressure of 21 kPa. In the lungs, it's slightly lower, perhaps 20 kPa, but in the microvasculature at the alveoli it drops to 13 kPa. In the circulation, it ranges from 13 kPa down to 5 kPa in the de-oxygenated veins. So the partial pressure of oxygen in individual cells within tissues, away from vessels, can be well below 5 kPa, depending on their distance from the vasculature. That gives a sense for normal oxygen levels, or normoxia. When cellular oxygen levels drop even further, producing hypoxia, the hypoxia inducible factor (HIF) alters gene expression as an adaptive response. HIF action is essential for preventing ischemia-reperfusion injury, critical for normal hematopoiesis and vascular development, and central to tumorigenesis.[1-3]

HIF-1α Action: The Basics

The HIF family of transcription factors acts as heterodimers of α and β subunits. There are three known isoforms of HIF-α: HIF-1α, HIF-2α, and HIF-3α.[4,5] All HIFs share similar N-terminal domains, consisting of a basic helix-loop-helix (HLH) region linked to a pair of period-ARNT-Sim (PAS) segments (Figure 1). The HIF-α isoforms also contain two oxygen-dependent degradation domains (ODDD) and HIF-1α and HIF-2α also contain a pair of transactivation domains (TAD). The lack of TADs on HIF-3α has led to the suggestion that this isoform competes with the other α isoforms. The β subunit is also known as the aryl hydrocarbon receptor nuclear translocator (ARNT).

HIF-1α is the best characterized isoform. Under normoxic conditions, oxygen activates prolyl hydroxylase (PHD) enzymes, which place hydroxyl groups on Pro^{402} and Pro^{564} of the ODDD domains.[6] While there are four isoforms of PHD, PHD2 has a higher affinity for HIF-1α. Hydroxylation of HIF-1α allows binding by the tumor suppressor von Hippel-Lindau protein (pVHL), which in turn binds Elongin C (EloC). This recruits an E3 ubiquitin-protein ligase complex, promoting Lys^{48}-targeted ubiquitination and proteasome-mediated degradation of HIF-1α. Through this regulatory mechanism, the levels of the α isoforms of HIF are low during normoxia.

During hypoxia, PHD is not activated, so HIF-1α protein levels increase. Nuclear import is facilitated by a nuclear import sequence (NIS), whose activity is enhanced by phosphorylation on Ser^{641} and Ser^{643} mediated by ERK2; the same phosphorylation also inhibits nuclear export. Within the nucleus HIF-1α heterodimerizes with HIF-1β and this complex binds, *via* the HLH elements, to a hypoxia response element (HRE) on specific genes. Transcriptional activity is influenced by co-factors like p300, which interact with HIF-1α at the C-terminal TAD. Binding of co-factors at this site are blocked by the action of Factor Inhibiting HIF (FIH), which hydroxylates Arg^{803} in the TAD. On the flip side, S-nitrosation by NO of Cys^{800} stimulates p300 binding and transcription.

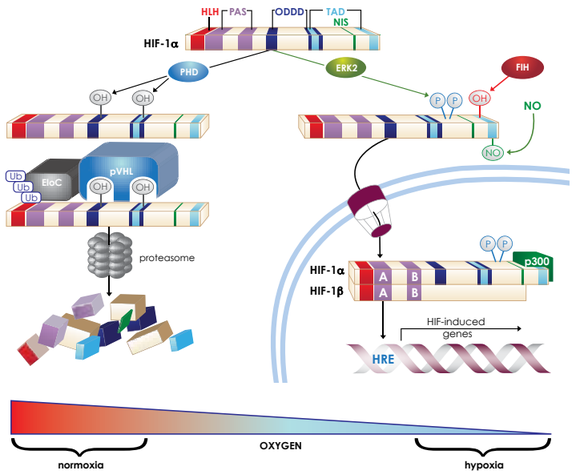


Figure 1. HIF-1α regulation

HIF-1α Action: Cytoplasmic Details

A more complete picture can be built around this basic framework.[7,8] For example, pVHL-mediated and ubiquitin-dependent degradation of HIF-1α can occur during normoxia. However, this process is blocked during hypoxia by the association of the heat shock protein HSP90 with HIF-1α (Figure 2). Inhibitors of HSP90, like geldanamycin (GA), allow breakdown of HIF-1α to proceed. Also, the protein receptor of activated C kinase (RACK1) can compete with HSP90 for binding to HIF-1α; when RACK1 wins, HIF-1α is destroyed.

The activity of the key enzyme PHD2 is modulated by a variety of factors in addition to oxygen (Figure 2). The osteosarcoma 9 protein (OS9) stabilizes the PHD2/HIF-1α interaction and in this way increases PHD2-mediated action.

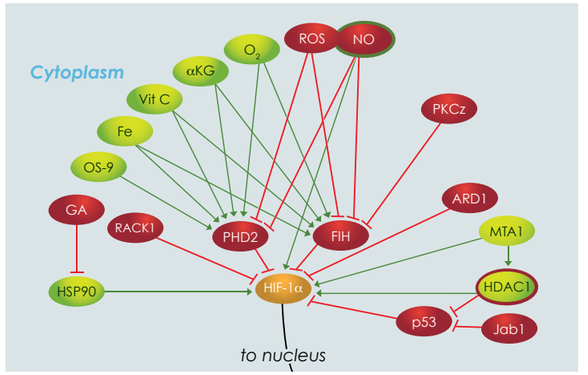


Figure 2. Cytoplasmic factors affecting HIF-1α

PHD2 depends on iron as Fe(II) as a co-factor. The activity of PHD2 is also stimulated by vitamin C (Vit C) and by α-ketoglutarate (αKG), both of which act as co-factors. Reactive oxygen species (ROS), which increase during hypoxia, inhibit PHD2, in part by converting Fe(II) to Fe(III). In addition to directly enhancing HIF-1α activity, NO can inhibit PHD2 by chelating Fe(II).[9]

Like PHD2, FIH is an iron-dependent enzyme whose activity is stimulated by oxygen and α-ketoglutarate. Also like PHD2, ROS and NO interfere with FIH action. In addition, the expression of FIH can be blocked by protein kinase C-zeta (PKCζ), which is constitutively active in some forms of cancer.

Other proteins have been found to interact with and modulate HIF-1α stability. For example, ADP-ribosylation factor domain protein (ARD1) has been found to interact with HIF-1α and promote the acetylation of Lys^{532}, enhancing pVHL binding, ubiquitination, and breakdown. Similarly, other enzymes with deacetylase activity, like histone deacetylase 1 (HDAC1), increase the stability and transcriptional activity of HIF-1α under hypoxic conditions. The protein metastasis associated 1 (MTA1) acts both as a deacetylase of HIF-1α and activator of HDAC and in these two ways increases HIF stability and transcriptional activity. Also, inhibitors of deacetylases, which typically allow widespread acetylation of proteins, trigger HIF-1α loss.

In hypoxic conditions, p53 interacts with HIF-1α and promotes ubiquitination and degradation. The binding of p53 can be blocked by Jun activation domain binding protein (Jab-1), which also can interact with the ODDD. Perhaps more interesting, deacetylation of p53 by HDAC promotes proteasomal degradation of p53, which contrasts with its stabilization action on HIF-1α.

HIF-1 Regulation: Nuclear Details

The details above indicate how the stabilization of the HIF-1α protein in the cytoplasm allows transcription to become possible.[10,11] Other proteins, found within the nucleus, increase HIF-1 transcriptional activity and also enhance HIF-1α protein stability. This suggests that, following release from the HRE, HIF-1α is exported from the nucleus and degraded. The proteins ID1 (inhibitor of DNA binding 1), HBX (hepatitis B virus X protein) and Trx-1 (thioredoxin-1) have been shown to increase both HIF-1α stability and transcription (Figure 3). ID1 is a dominant negative HLH protein that commonly inhibits other proteins with basic HLH domains (like HIF), but increases HIF activity in cancer cells. HBX is a viral transcriptional co-activator that stimulates transcription activity of HIF-1 as well as that of viral transcription factors. Trx-1 is a small redox protein that is overexpressed in many human primary tumors; in these settings, it increases HIF activity and stability.

Several proteins have been shown to directly interact with HIF-1 in the nucleus under hypoxic conditions. For example, p300, or the related CREB binding protein (CBP), directly binds HIF-1α at the C-terminal TAD. These enzymes have histone acetyltransferase (HAT) activity, which helps promote transcription. They also act as adaptor molecules, allowing other proteins to bind to the DNA/HIF-1 complex. Suggesting that the HAT activity is important, HIF-1α transcriptional activity is also increased by HDAC7, by the steroid receptor coactivator SRC1, and by transcription intermediary factor 2 (TIF-2), all of which have HAT activity and bind HIF-1α.

The p300 protein appears to play a critical role in the assembly of the transcriptional complex. As noted above, FIH inhibits HIF-1α by modifying it so that p300 can't bind. This suggests that p300 is necessary for HIF-1α transcriptional activity. Another protein, CITED2 (CBP/p300 interacting coactivator with glutamic acid/aspartic acid-rich tail 2), reduces HIF activity by competing with p300 for binding. Experiments using interfering RNA for p300 indicate that p300 is necessary for SRC1 binding to HIF-1. These findings underline the importance of p300 as an adaptor protein.

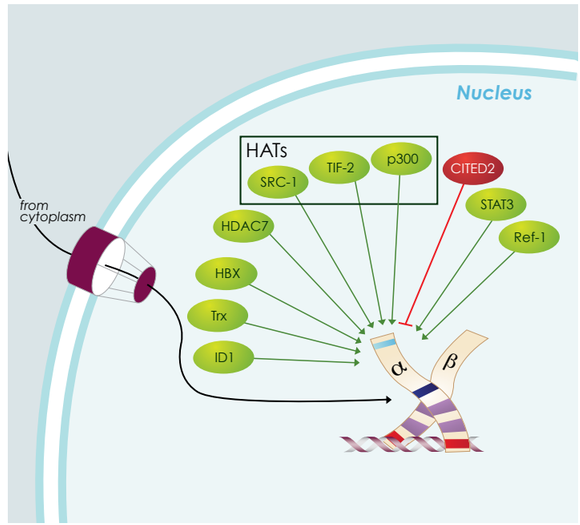


Figure 3. Regulation of HIF-1α/β transcription

The proteins STAT3 (signal transducer and activator of transcription 3) and Ref-1 (redox-factor-1) also associate with, and stimulate, the HIF-1 transcriptional complex, in association with p300. STAT3 is activated by cytokines and growth factors, including IFN, EGF, and IL-6, suggesting that these signaling compounds may augment HIF-mediated gene expression. The way in which STAT3 and Ref-1 enhance transcription remains to be determined. n

Due to space limitations, the reader is encouraged to consult recent reviews for additional information.[3,5,8,12]

Reference List

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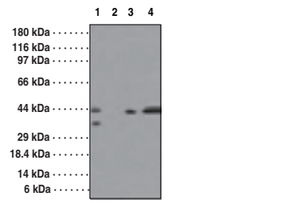
SMAD3 Polyclonal Antibody 10832

Protein G-purified IgG **Stability:** ≥6 months at -20°C
Summary: Antigen: human SMAD3 amino acids 100-150 • Host: rabbit • Cross Reactivity: (+) bovine, canine, human, mouse, porcine, rat, and Rhesus monkey SMAD3 • Application(s): IHC, WB • SMAD3 is a receptor-regulated SMAD (R-SMAD) that functions downstream of TGF-β and activin receptors and mediates their signaling. It is recruited by SARA (SMAD anchor for receptor activation) to the receptor kinase for phosphorylation. Upon phosphorylation it plays role in cell proliferation, differentiation, apoptosis and formation of extracellular matrix.

100 µg

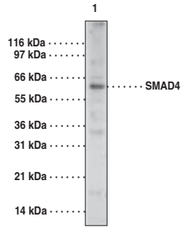


Lane 1: Human liver lysate (absence of immunizing peptide)
Lane 2: Human liver lysate (presence of immunizing peptide)
Lane 3: Murine liver lysate (absent peptide)
Lane 4: Rat liver lysate (absent peptide)

SMAD4 Polyclonal Antibody 10838

Protein G-purified IgG **Stability:** ≥6 months at -20°C
Summary: Antigen: human SMAD4 amino acids 186-199 and 509-523 • Host: rabbit • Cross Reactivity: (+) human, New World monkey, mouse, and rat SMAD4 • Application(s): WB • SMAD4 is a common-mediator SMAD (co-SMAD) that is part of a family of intracellular proteins that are essential components in the signaling pathways of the Ser/Thr kinase receptors of the transforming growth factor β superfamily.

100 µg

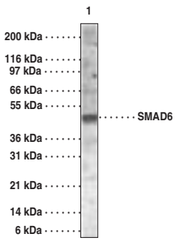


Lane 1: A549 cell lysate (15 µg)

SMAD6 Polyclonal Antibody 10839

Protein G-purified IgG **Stability:** ≥6 months at -20°C
Summary: Antigen: human SMAD6 amino acids 85-99 and 372-388 • Cross Reactivity: (+) human, New World monkey, mouse, rat, and ovine SMAD6 • Application(s): IHC, WB • SMAD6 is an inhibitory SMAD (I-SMAD) that is part of a family of intracellular proteins that are essential components in the signaling pathways of the Ser/Thr kinase receptors of the transforming growth factor β superfamily.

100 µg

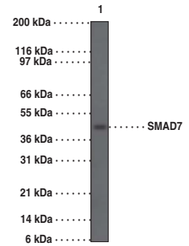


Lane 1: Jurkat cell lysate (30 µg) using SMAD6 antibody (2 µg/ml)

SMAD7 Polyclonal Antibody 10845

Protein G-purified IgG **Stability:** ≥6 months at -20°C
Summary: Antigen: human SMAD7 amino acids 12-29 and 36-50 • Host: rabbit • Cross Reactivity: (+) human, mouse, rat, and ovine SMAD7 • Application(s): WB • SMAD7 is an inhibitory SMAD (I-SMAD) that is part of a family of intracellular proteins that are essential components in the signaling pathways of the Ser/Thr kinase receptors of the transforming growth factor β superfamily.

100 µg

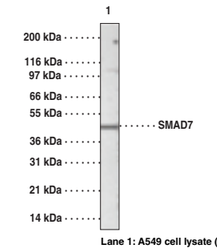


Lane 1: HepG2 cell lysate

SMAD7 Polyclonal Antibody (azide-free) 10840

Protein G-purified IgG **Stability:** ≥6 months at -20°C
Summary: Antigen: human SMDA7 amino acids 12-29 and 36-50 • Host: rabbit • Cross Reactivity: (+) human, mouse, and rat SMAD7 • Application(s): WB • SMAD7 is an inhibitory SMAD (I-SMAD) that is part of a family of intracellular proteins that are essential components in the signaling pathways of the Ser/Thr kinase receptors of the transforming growth factor β superfamily.

100 µg

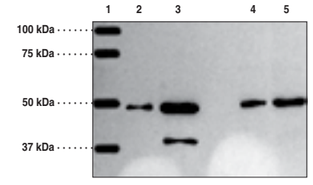


Lane 1: A549 cell lysate (15 µg)

Sphingosine Kinase 1 Polyclonal Antibody 10006822

SPHK 1
Peptide affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human SPHK 1 amino acids 264-274 • Host: rabbit • Cross Reactivity: (+) human and mouse SPHK 1, expected to react with rat SPHK 1 • Application(s): WB and ICC • SPHK 1 catalyzes the phosphorylation of SP to S1P. This reaction plays an important role in determining cell proliferation *versus* cell death.

1 ea



Lane 1: Precision Plus Protein Standard
Lane 2: SPHK 1 transfected cell lysates (10 µg)
Lane 3: SPHK 1 transfected cell lysates (20 µg)
Lane 4: Mouse heart homogenate (25 µg)
Lane 5: Mouse heart homogenate (50 µg)

•Also Available: **Sphingosine Kinase 1 Blocking Peptide** (10006823)

Sphingosine Kinase 1 Polyclonal FITC Antibody 10012201

SPHK 1
Fluorescein-conjugated affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human SPHK 1 amino acids 264-274 • Host: rabbit • Cross Reactivity: (+) mouse and human SPHK 1, expected to react with rat SPHK 1 • Application(s): FC, IF, and WB • SPHK 1 catalyzes the phosphorylation of SP to S1P, a key lipid mediator that plays an important role in determining cell proliferation *versus* cell death.

500 µl

Ubiquitin Monoclonal Antibody (Clone 5B9-B3) 13722

Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: native bovine ubiquitin conjugated to KLH • Isotype: $IgG_{2aκ}$ • Host: mouse, clone S5B9-B3 • Cross Reactivity: (+) human, mouse, rat, and bovine ubiquitin • Application(s): ELISA and WB • Ubiquitin functions to clear abnormal, foreign and improperly folded proteins by targeting them for degradation by the 26S proteosome. The ubiquitination process participates in the internalization and degradation of plasma membrane proteins and also plays a role in regulating signal transduction cascades through the elimination of inhibitor proteins.

50 µg
200 µg

Ubiquitin Monoclonal Antibody (Clone 6C11-B3) 13723

Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: native bovine ubiquitin conjugated to KLH • Isotype: $IgG_{2aκ}$ • Host: mouse, clone 6C11-B3 • Cross Reactivity: (+) human, mouse, rat, and bovine ubiquitin • Application(s): ELISA and WB • Ubiquitin functions to clear abnormal, foreign and improperly folded proteins by targeting them for degradation by the 26S proteosome. The ubiquitination process participates in the internalization and degradation of plasma membrane proteins and also plays a role in regulating signal transduction cascades through the elimination of inhibitor proteins.

50 µg
200 µg

Ubiquitin Polyclonal Antibody 13724

Rabbit serum **Stability:** ≥1 year at -20°C
Summary: Antigen: native bovine ubiquitin conjugated to KLH • Host: rabbit • Cross Reactivity: (+) human, monkey, mouse, rat, hamster, rabbit, guinea pig, bovine, porcine, canine, ovine, chicken, *Xenopus*, yeast, *Drosophila*, and rainbow trout ubiquitin • Application(s): ChIP, IP, and WB • Ubiquitin functions to clear abnormal, foreign and improperly folded proteins by targeting them for degradation by the 26S proteosome. The ubiquitination process participates in the internalization and degradation of plasma membrane proteins and also plays a role in regulating signal transduction cascades through the elimination of inhibitor proteins.

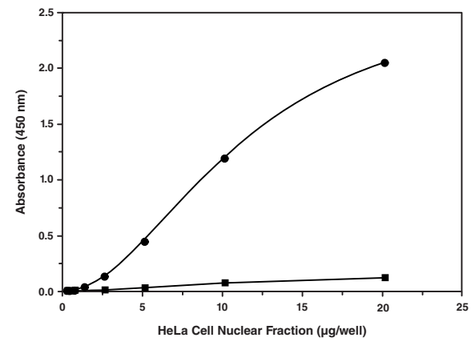
50 µg
200 µg

Assay Kits

ATF2 (Phospho-Thr^{69,71}) Transcription Factor Assay Kit 600130

Activating Transcription Factor 2
Stability: ≥6 months at -80°C
Summary: ATF2 is a sequence-specific DNA-binding protein belonging to the basic leucine zipper domain family of transcription factors that bind with high affinity to the octameric CRE. ATF2 mediates both transcription and DNA damage control through its phosphorylation/activation in response to inflammatory cytokines, UV irradiation, alkylating compounds, and other cellular stressors.

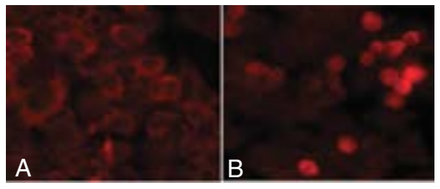
96 wells



ChREBP Cell-Based Translocation Assay Kit 10010060

Carbohydrate Response Element-Binding Protein
Stability: ≥1 year at -20°C
Summary: The identification of ChREBP activators is of great interest for drug discovery. The distinct translocation of the protein from the cytoplasm to the nucleus during activation makes it possible to study modulators of ChREBP through sub-cellular localization of the protein using conventional immunocytochemical staining with a specific antibody. Cayman's ChREBP Cell-Based Translocation Assay provides a highly specific ChREBP primary antibody together with a Dylight™ (product of Thermo Scientific) conjugated secondary antibody in a ready to use format.

96 wells

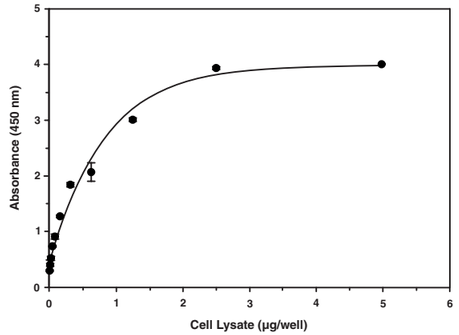


Translocation of ChREBP into nuclei induced by 10 mg/ml sucrose. HepG2 cells were seeded in a 96-well plate at a density of 3 x 10^4 cells/well and cultured overnight. The next day, cells were treated with PBS (vehicle) or 10 mg/ml sucrose in PBS for 24 hours. *Panel A:* Cells treated with PBS alone demonstrate cytoplasmic localization of ChREBP, indicating that most cells have inactive protein. *Panel B:* Sucrose treatment for 24 hours induces ChREBP translocation into the nuclei, indicating activation of the protein.

ChREBP Transcription Factor Assay Kit 10006909

Carbohydrate Response Element-Binding Protein
Stability: ≥6 months at -80°C
Summary: ChREBP is a transcription factor playing a critical role in the nutrient and hormonal regulation of genes encoding enzymes of glucose metabolism and lipogenesis pathways.

96 wells



CREB (Phospho-Ser[133]) Transcription Factor Assay Kit 10009846

cAMP-Response Element-Binding Protein
Stability: ≥1 year at -80°C
Summary: CREB is a transcription factor that binds to cAMP-responsive element (CRE) promoter sites to regulate the transcription of numerous genes involved in metabolic regulation, depression, long term memory, and other physiological processes. Phosphorylation on serine 133 (Ser[133]) activates CREB to induce transcription of target genes. Diverse stimuli such as growth factors, neurotransmitters, hypoxia, growth factors, UV light, survival signals, and stress signals are some of the known activators of CREB. Cayman's CREB (Phospho-Ser[133]) Transcription Factor Assay is a non-radioactive, sensitive method for detecting CREB DNA binding activity in nuclear extracts or whole cell lysates.

96 wells

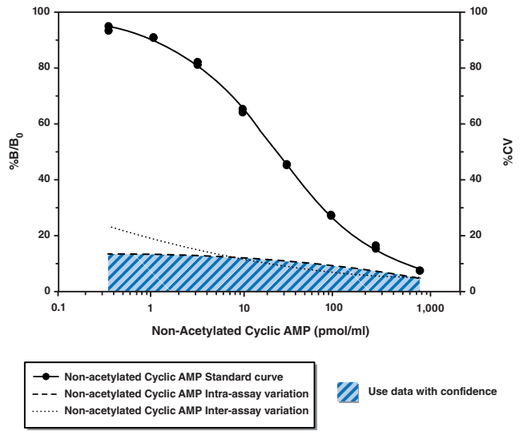
Cyclic AMP EIA Kit 581001

Adenosine 3',5'-cyclic mononucleotide, cAMP
Stability: ≥1 year at -20°C
Sensitivity: 50% B/B_0: 20.4 pmol/ml (non-acetylated); 0.5 pmol/ml (acetylated)
80% B/B_0: 3.1 pmol/ml (non-acetylated); 0.1 pmol/ml (acetylated)
Summary: cAMP is a ubiquitous cellular second messenger that is a critical component of a signal transduction pathway linking membrane receptors and their ligands to the activation of internal cellular enzymatic activity and gene expression.
Specificity:

Non-Acetylated		Acetylated	
cAMP	100%	Acetylated cAMP	100%
cGMP	1.5%	Acetylated cGMP	0.69%

For a full specificity profile, please go to www.caymanchem.com

96 solid/strip wells
480 solid/strip wells



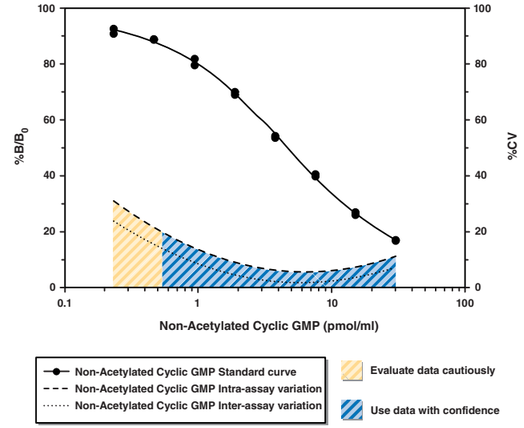
Cyclic GMP EIA Kit 581021

cGMP, Guanosine 3',5'-cyclic mononucleotide
Stability: ≥1 year at -20°C
Sensitivity: 50% B/B_0: 4.6 pmol/ml (non-acetylated); 0.46 pmol/ml (acetylated)
80% B/B_0: 1 pmol/ml (non-acetylated); 0.1 pmol/ml (acetylated)
Summary: Cayman's cGMP Assay is a competitive EIA that can be used for quantification of cGMP directly obtained from cell lysates, tissue homogenates, plasma or urine. Since the antibody used in this assay was prepared against a cGMP-carrier protein conjugate, antibody binding is increased if an acetyl group is present on the 2' hydroxyl group of the cGMP. The optional acetylation procedure for both samples and standards increases the sensitivity of the assay approximately 10 fold.
Specificity:

Non-Acetylated		Acetylated	
cGMP	9%	Acetylated cGMP	100%
Dibutyryl cGMP	0.8%	Acetylated cAMP	0.05%

For a full specificity profile, please go to www.caymanchem.com

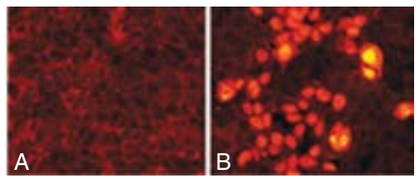
96 solid/strip wells
480 solid/strip wells



ERK/MAPK (Phospho-Thr[202]/Tyr[204]) Cell-Based Phosphorylation/Translocation Assay Kit 10010549

Stability: ≥1 year at -20°C
Summary: Cayman's ERK/MAPK (Phospho-Thr[202]/Tyr[204]) Cell-Based Phosphorylation/Translocation Assay provides the tools necessary to study ERK/MAPK phosphorylation and translocation within whole cells. The kit contains a phospho-specific ERK/MAPK (Phospho-Thr[202] and Tyr[204]) primary antibody together with a Dylight™ (product of Thermo Scientific) conjugated secondary antibody in a ready-to-use format. Tamoxifen, which has been shown by scientists at Cayman Chemical to cause the translocation of phosphorylated ERK/MAPK (Phospho-Thr[202]/Tyr[204] between the cytoplasm and nuclear compartments, is included as a positive control.

1 ea

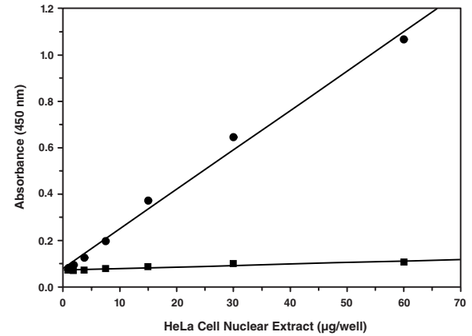


Tamoxifen induces the translocation of ERK/MAPK (Phosopho-Thr[202]/Tyr[204]) from the cytoplasm to the nucleus in MCF-7 cells. Cells were plated at 1 x 10^5 cells/well in a 96-well plate and grown in DMEM containing 10% FBS overnight. *Panel A:* Cells were then treated with vehicle *Panel B:* 20 µM tamoxifen for 20 minutes. The cells were processed for immunostaining with the ERK/MAPK (Phosopho-Thr[202]/Tyr[204]) antibody following the immunofluorescent staining protocol described above. Translocation of the phosphorylated ERK from the cytoplasm to the nucleus by tamoxifen treatment is evident.

HIF-1α Transcription Factor Assay Kit 10006910

Hypoxia Inducible Factor-1α
Stability: ≥6 months at -80°C
Summary: The HIF (hypoxia-inducible factor) transcription factor is a member of the basic-helix-loop-helix (bHLH) family of transcription factors and plays an important role in maintaining cellular oxygen homeostasis. HIF-1α has emerged as an important drug target in breast and prostate cancer, cardiovascular disease, and ischemia. Cayman's HIF-1α Transcription Factor Assay is a sensitive ELISA-based method for detecting HIF-1α DNA binding activity in nuclear extracts and whole cell lysates.

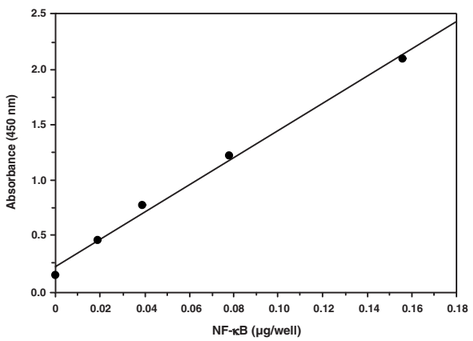
96 wells



NF-κB (human p50) Transcription Factor Assay Kit 10006912

Stability: ≥6 months at -80°C
Summary: The NF-κB/Rel family of transcription factors is comprised of several structurally-related proteins that form homodimers and heterodimers and include p50/p105, p52/p100, RelA (p65), and c-Rel/NF-κB. Acting as dimers, these transcription factors bind to κB sites on DNA, thereby regulating expression of target genes. The most common Rel/NF-κB dimer in mammals contains p50-RelA (p50/p65) heterodimers and is an attractive target for potential therapeutics in human inflammation and certain other diseases. Cayman's NF-κB (human p50) Transcription Factor Assay is a non-radioactive, sensitive method for detecting human NF-κB (p50) DNA binding activity in nuclear extracts and whole cell lysates. It will not cross-react with NF-κB (p65).

96 wells

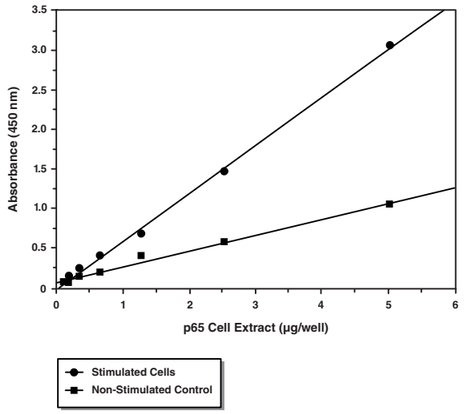


NF-κB (human p50/p65) Combo Transcription Factor Assay Kit 10011223

Stability: ≥6 months at -80°C

Summary: The NF-κB/Rel family of transcription factors is comprised of several structurally-related proteins that form homodimers and heterodimers and include p50/p105, p52/p100, RelA (p65), and c-Rel/NF-κB. Acting as dimers, these transcription factors bind to κB sites on DNA, thereby regulating expression of target genes. The most common Rel/NF-κB dimer in mammals contains p50-RelA (p50/p65) heterodimers and is an attractive target for potential therapeutics in human inflammation and certain other diseases. Cayman's NF-κB (human p50/p65) Combo Transcription Factor Assay is a non-radioactive, sensitive method for detecting p50 and p65 transcription factor DNA binding activity in nuclear extracts.

96 wells

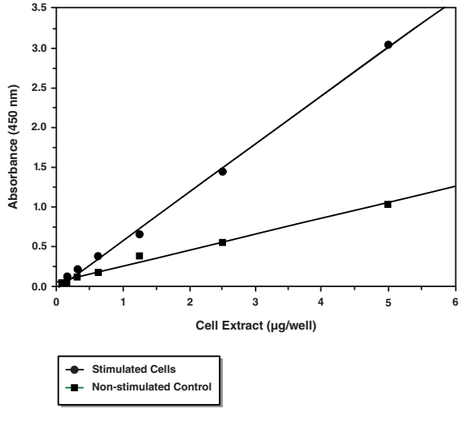


NF-κB (p65) Transcription Factor Assay Kit 10007889

Stability: ≥6 months at -80°C

Summary: The NF-κB/Rel family of transcription factors is comprised of several structurally-related proteins that form homodimers and heterodimers and include p50/p105, p52/p100, RelA (p65), and c-Rel/NF-κB. Acting as dimers, these transcription factors bind to κB sites on DNA, thereby regulating expression of target genes. The most common Rel/NF-κB dimer in mammals contains p50-RelA (p50/p65) heterodimers and is an attractive target for potential therapeutics in human inflammation and certain other diseases. Cayman's NF-κB (p65) Transcription Factor Assay is a non-radioactive, sensitive method for detecting human NF-κB (p65) DNA binding activity in nuclear extracts and whole cell lysates. It will not cross-react with NF-κB (p50).

96 wells

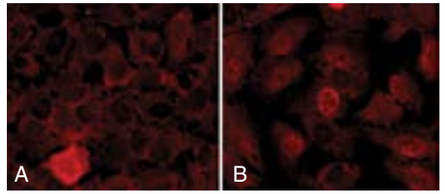


p38 MAPK (Phospho-Thr^{180}/Tyr^{182}) Cell-Based Phosphorylation/Translocation Assay Kit 10010374

Stability: ≥1 year at -20°C

Summary: Phosphorylation/Translocation Assay provides a highly specific phospho-p38 MAPK (phospho-Thr^{180} and Tyr^{182}) primary antibody together with a DyLight™ (product of Thermo Scientific) conjugated secondary antibody in a ready-to-use format. Thrombin, which has been shown by scientists at Cayman Chemical to cause the translocation of phospho-p38 MAPK (phospho-Thr^{180} and Tyr^{182}) into nuclei, is included as a positive control.

1 ea



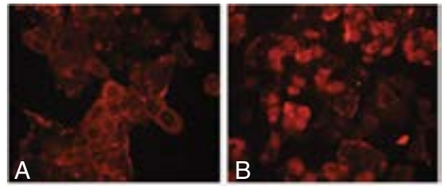
Thrombin-induced translocation of p38 MAPK (Phospho-Thr^{180}/Tyr^{182}) in HeLa cells. *Panel A:* HeLa cells were treated with vehicle or *Panel B:* thrombin 10 U/ml for three hours, then fixed and stained with p38 MAPK (phospho-Thr^{180}/Tyr^{182}) primary antibody. The staining was visualized using a goat anti-rabbit antibody conjugated to DyLight™ 549. Translocation of the phospho-Thr^{180}/Tyr^{182} p38 from the cytoplasm to nuclei upon stimulation by thrombin is evident.

p53 Cell-Based Activation/Translocation Assay Kit 600008

Stability: ≥6 months at -20°C

Summary: The tumor suppressor protein p53 plays a crucial role in coordinating cellular responses to genotoxic stress and holds many important clinical implications in the treatment of cancer. Cayman's p53 Cell-Based Activation/Translocation Assay provides a highly specific p53 primary monoclonal antibody together with a DyLight™ (product of Thermo Scientific) conjugated secondary antibody in a ready-to-use format. (-)-Nutlin-3, a potent inhibitor of Mdm2-p53 interaction, which has been shown by scientists at Cayman to cause the activation and translocation of p53 between the cytoplasm and nuclear compartments, is included as a positive control.

96 wells



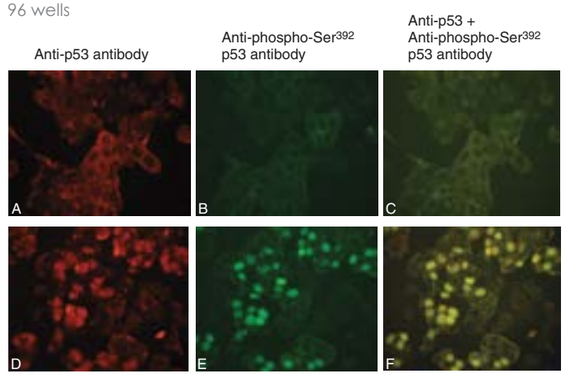
(-)-Nutlin-3-induced translocation of p53 in MCF-7 cells. *Panel A*: MCF-7 cells were treated with vehicle or *Panel B*: 50 µM (-)-Nutlin-3 for four hours, then fixed and stained with p53 monoclonal antibody according to the protocol described in the booklet. Translocation of p53 from cytoplasm to nuclei upon stimulation by (-)-Nutlin-3 is evident.

p53 Total and p53 (Phospho-Ser^{392}) Dual Staining Assay Kit 600060

Stability: ≥6 months at -20°C

Summary: Cayman's p53 Total and p53 (Phospho-Ser^{392}) Dual Staining Assay provides a pair of highly specific antibodies against total and phospho-p53 (Phospho-Ser^{392}) together with a pair of matched DyLight™ (product of Thermo Scientific) conjugated secondary antibodies in a ready-to-use format. (-)-Nutlin-3, a potent inhibitor of Mdm2-p53 interaction which has been shown to cause the activation and translocation of p53 between the cytoplasm and nuclear compartments, is included as a positive control.

96 wells



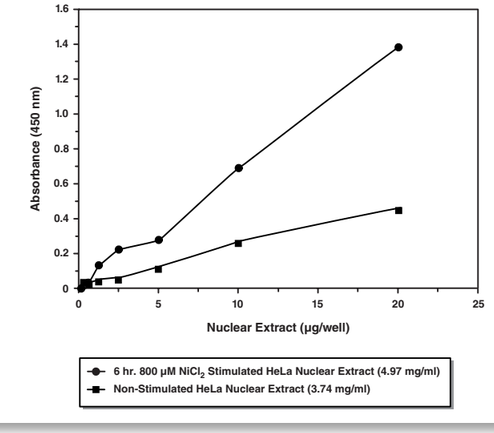
(-)-Nutlin-3-induced translocation of p53 in MCF-7 cells. MCF-7 cells were treated with vehicle (top panels) or 50 µM (-)-Nutlin-3 (bottom panels) for four hours, then fixed and stained as described in the assay protocol. Panel A and B shows that in unstimulated MCF-7 cells, most of p53 was not phosphorylated and appeared as cytoplasmic staining (strong staining of total protein in A and weak staining of phosphorylated protein in B). Panel C is the merged image of A and B. In contrast, panel D and E shows that upon stimulation by (-)-Nutlin-3, most of p53 was phosphorylated and appeared in the nucleus (strong staining of both total protein and phosphorylated protein in both D and E, respectively). Panel F is the merged image of D and E.

p53 Transcription Factor Assay Kit 600020

Stability: ≥1 year at -80°C

Summary: The tumor suppressor protein p53 plays a crucial role in coordinating cellular responses to genotoxic stress and holds many important clinical implications in the treatment of cancer. Cayman's p53 Transcription Factor Assay is a non-radioactive, sensitive method for detecting specific transcription factor DNA binding activity in nuclear extracts. A specific double-stranded DNA (dsDNA) sequence containing the p53 response element is immobilized onto the wells of a 96-well plate. p53 contained in a nuclear extract, binds specifically to the p53 response element and is detected by addition of a specific primary antibody directed against p53. A secondary antibody conjugated to HRP is added to provide a sensitive colorimetric readout at 450 nm.

96 wells

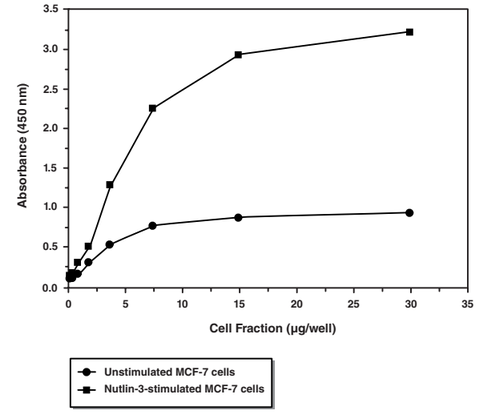


p53 Designer Transcription Factor Assay Kit 600030

Stability: ≥1 year at -80°C

Summary: Cayman's p53 Designer Transcription Factor Assay is designed to study alternate p53 DNA-binding sites. A biotinylated oligonucleotide is incubated with p53 contained in a nuclear extract; this mixture then binds to the streptavidin plate provided in the kit. p53 is detected by addition of a specific primary antibody directed against p53. A secondary antibody conjugated to HRP is added to provide a sensitive colorimetric readout at 450 nm.

96 wells



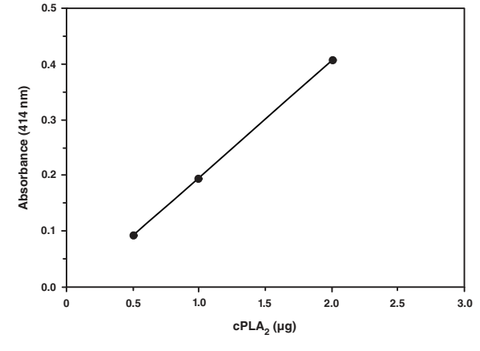
cPLA$_2$ Assay Kit 765021

Calcium-dependent cytosolic PLA$_2$, PLA$_2$ Type IV

Stability: ≥1 year at -20°C

Summary: Arachidonoyl thio-PC is a substrate for cPLA$_2$ by virtue of the presence of arachidonic acid at the *sn*-2 position of the glycerophospholipid. Hydrolysis of the arachidonoyl thioester bond at the *sn*-2 position by PLA$_2$ releases free thiol which can be detected by 5,5'-dithio-*bis*(2-nitrobenzoic acid). This assay can be used to determine the activity of cPLA$_2$ in purified preparations, cell cultures, or tissue homogenates that are known to contain only cPLA$_2$. Use of this assay with preparations containing more than one type of PLA$_2$ will result in the measurement of total PLA$_2$ activity rather than cPLA$_2$ alone. Isozyme-specific cPLA$_2$ activity can be measured by excluding sPLA$_2$ or inhibiting iPLA$_2$ activities in the assay.

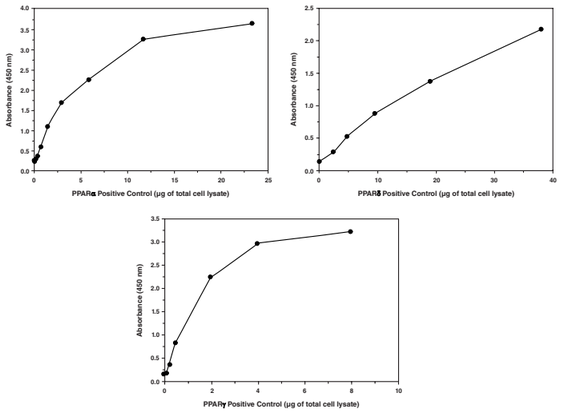
96 wells



PPARα, δ, γ Complete Transcription Factor Assay Kit 10008878

Peroxisome Proliferator-activated Receptor α, δ, γ
Stability: ≥1 year at -80°C
Summary: PPARs are ligand-activated transcription factors belonging to the large superfamily of nuclear receptors. PPARα primarily activates genes encoding proteins involved in fatty acid oxidation, while PPARγ primarily activates genes directly involved in lipogenic pathway and insulin signaling. Members of the PPAR family are important direct targets of many antidiabetic and hypolipidemic drugs. Cayman's PPAR Transcription Factor Assays are a non-radioactive, sensitive method for detecting specific transcription factor DNA binding activity in nuclear extracts and whole cell lysates.

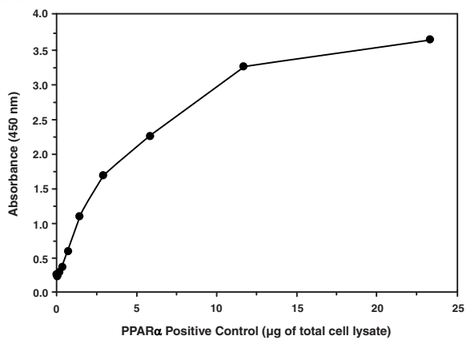
96 wells



PPARα Transcription Factor Assay Kit 10006915

Peroxisome Proliferator-activated Receptor α
Stability: ≥6 months at -80°C
Summary: PPARs are ligand-activated transcription factors belonging to the large superfamily of nuclear receptors. PPARα primarily activates genes encoding proteins involved in fatty acid oxidation, while PPARγ primarily activates genes directly involved in lipogenic pathway and insulin signaling. Members of the PPAR family are important direct targets of many antidiabetic and hypolipidemic drugs. Cayman's PPAR Transcription Factor Assays are a non-radioactive, sensitive method for detecting specific transcription factor DNA binding activity in nuclear extracts and whole cell lysates.

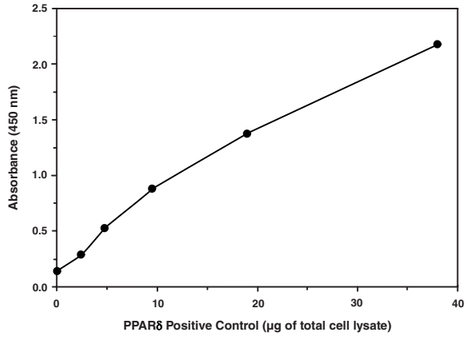
96 wells



PPARδ Transcription Factor Assay Kit 10006914

Peroxisome Proliferator-activated Receptor δ
Stability: ≥6 months at -80°C
Summary: PPARs are ligand-activated transcription factors belonging to the large superfamily of nuclear receptors. PPARα primarily activates genes encoding proteins involved in fatty acid oxidation, while PPARγ primarily activates genes directly involved in lipogenic pathway and insulin signalling. Members of the PPAR family are important direct targets of many antidiabetic and hypolipidemic drugs. Cayman's PPAR Transcription Factor Assays are a non-radioactive, sensitive method for detecting specific transcription factor DNA binding activity in nuclear extracts and whole cell lysates.

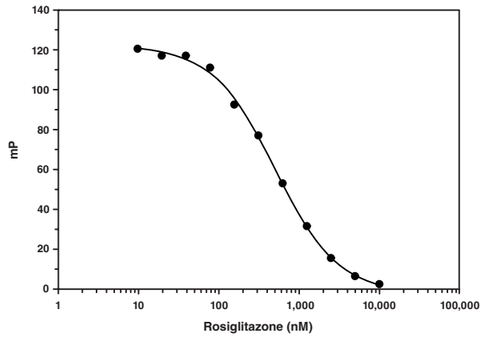
96 wells



PPARγ Ligand Screening Assay Kit 10007685

Peroxisome Proliferator-activated Receptor γ
Stability: ≥6 months at -80°C
Summary: Cayman's PPARγ FP-Based Ligand Screening Assay - Green provides a convenient FP-based single step assay for screening PPARγ ligands. In this assay, a ligand of PPARγ was conjugated to FITC and is used as the displacement probe. Agonists and antagonists of PPARγ will displace the fluorescent probe leading to a decrease in FP. The PPARγ FP-Based Ligand Screening Assay is a robust assay with a Z' factor of 0.81 and has a dynamic range of greater than 120 mP units. The assay has been validated using known agonists/ligands of PPARγ (Arachidonic Acid, Rosiglitazone, Troglitazone, etc.) with IC_{50} values ranging from nanomolar to millimolar concentrations.

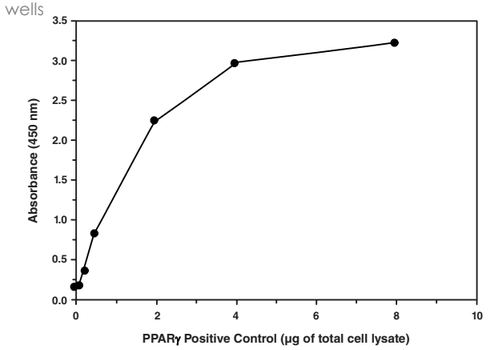
384 wells



PPARγ Transcription Factor Assay Kit 10006855

Peroxisome Proliferator-activated Receptor γ
Stability: ≥6 months at -80°C
Summary: PPARs are ligand-activated transcription factors belonging to the large superfamily of nuclear receptors. PPARα primarily activates genes encoding proteins involved in fatty acid oxidation, while PPARγ primarily activates genes directly involved in lipogenic pathway and insulin signaling. Members of the PPAR family are important direct targets of many antidiabetic and hypolipidemic drugs. Cayman's PPAR Transcription Factor Assays are a non-radioactive, sensitive method for detecting specific transcription factor DNA binding activity in nuclear extracts and whole cell lysates.

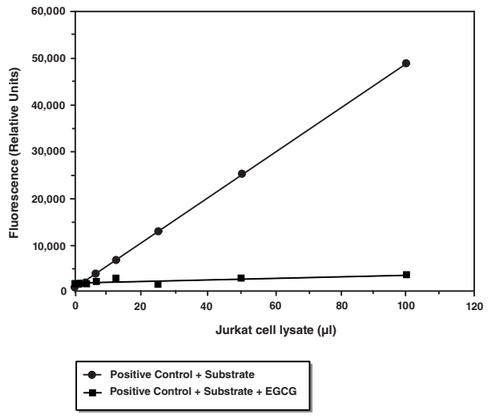
96 wells



20S Proteasome Assay Kit 10008041

Stability: ≥6 months at -80°C
Summary: The proteasome is a multicatalytic proteinase complex that is involved in the selective degradation of intracellular proteins. The 20S proteasome is the proteolytic core of a large protein degradation complex, the 26S proteasome. Proteasome inhibitors exhibit anti-inflammatory and antiproliferative effects, evidence that the proteasome may be an important drug target for the treatment for cancer and inflammatory diseases. Cayman's 20S Proteasome Assay employs a specific 20S substrate, SUC-LLVY-AMC which, upon cleavage by the active enzyme, generates a highly fluorescent product with an emission wavelength at 480 nm. The kit is easy to use and can be easily adapted to high throughput screening for therapeutic compounds regulating activation of the 20S proteasome.

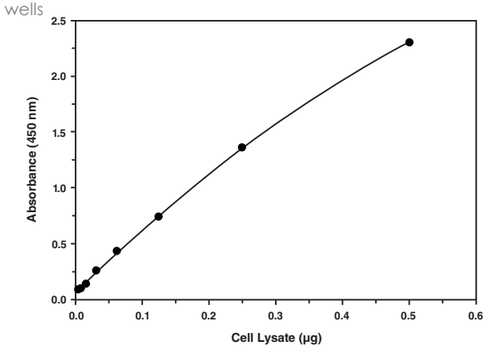
1 ea



SREBP-1 Transcription Factor Assay Kit 10010854

Sterol Regulatory Element-Binding Protein-1
Stability: ≥1 year at -80°C
Summary: Three known isoforms of SREBP transcription factors have been characterized: SREBP-1a, SREBP-1c, and SREBP-2. SREBP-1c acts primarily to activate genes required for fatty acid synthesis, such as acetyl CoA carboxylase, fatty acid synthase, and long chain fatty acid elongase. In addition, SREBP-1c may also contribute to the regulation of glucose uptake and synthesis through induction of glucokinase. SREBP-1c has important clinical implications in the treatment of many diseases including obesity, diabetes mellitus, insulin resistance, and non-alcoholic fatty liver disease.

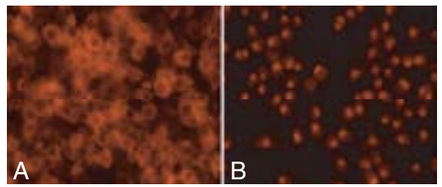
96 wells



SREBP-2 Cell-Based Translocation Assay Kit 10009239

Sterol Regulatory Element-Binding Protein-2
Stability: ≥1 year at -20°C
Summary: SREBP-2 is a transcription factor that regulates cholesterol synthesis by activating the expression of genes for HMG-CoA reductase and other enzymes of the cholesterol synthetic pathway. Cayman's SREBP-2 Cell-Based Translocation Assay Kit provides the tools needed to study SREBP-2 movement within whole cells. The kit contains a highly specific SREBP-2 primary antibody together with a DyLight™ (trademarked by Thermo Scientific) conjugated secondary antibody in a ready to use format. Also included as a positive control is a cholesterol trafficking inhibitor, U18666A, which has been shown to activate SREBP-2 translocation into nuclei by scientists at Cayman Chemical Company.

96 wells

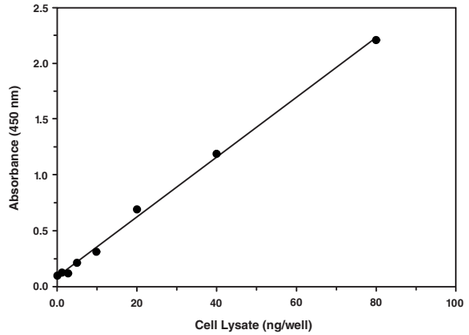


Translocation of SREBP-2 into nuclei by 24 µM U-18666A. Raw 264.7 cells were seeded in a 96-well plate at a density of 3 x 10^4 cells/well and cultured overnight. The next day, cells were treated with DMSO (vehicle) or 24 µM U-18666A for 72 hours. *Panel A*: Cells treated with DMSO alone demonstrate cytoplasmic localization of SREBP-2, indicating that most of cells have inactive protein. *Panel B*: U-18666A treatment for three days induced SREBP-2 translocation into the nuclei, indicating that blockage of cholesterol transport in these cells activates the protein.

SREBP-2 Transcription Factor Assay Kit 10007819

Sterol Regulatory Element-Binding Protein-2
Stability: ≥6 months at -80°C
Summary: SREBP-2 is a transcription factor that performs a critical role in the transcriptional regulation of genes involved in cholesterol synthesis and uptake including HMG-CoA synthase, HMG-CoA reductase, and the LDL receptor.

96 wells



•Also Available: **SREBP-2 Western Ready Control** (10009749)

Proteins

ChREBP DBD (human recombinant) 10009524

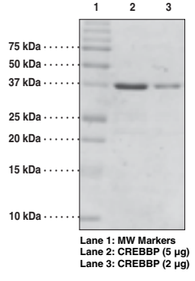
Carbohydrate Response Element-binding Protein DNA Binding Domain, GenBank Accession No. BC012925, Williams-Beuren Syndrome Chromosome Region 14, WS-bHLH
M_r: ~38.3 kDa **Purity:** ≥85% **Stability:** ≥6 months at -80°C
Source: Recombinant GST-tagged ChREBP amino acids 648-741 expressed in *E. coli* • Under conditions of low glucose, ChREBP is phosphorylated which sequesters the transcription factor in the cytoplasm. Under conditions of elevated glucose, one of its metabolites, xylulose 5-phosphate, activates Protein Phosphatase 2A which dephosphorylates ChREBP. Dephosphorylated ChREBP translocates into the nucleus where it is further dephosphorylated, which allows ChREBP to bind to the carbohydrate response element within the promoter of the L-type pyruvate kinase gene. Cayman's ChREBP DBD contains amino acids 648-741 of the full length protein fused to GST at the N-terminus.

5 µg
10 µg
25 µg

CREB-binding protein bromodomain (human recombinant) 11288

cAMP-Response Element-binding Protein 1 CREB-1, CBP, CREBBP
M_r: 40.8 kDa **Purity:** ≥95% **Stability:** ≥1 year at -80°C
Source: Recombinant N-terminal GST-tagged protein expressed in *E. coli* • CREBBP bromodomain has been shown to modulate the stability and function of the tumor suppressor protein p53. CREBBP bromodomain recognizes the acetylated lysine residue 382 on p53.

25 µg
50 µg
100 µg



Lane 1: MW Markers
Lane 2: CREBBP (5 µg)
Lane 3: CREBBP (2 µg)

NF-κB (p50) (human recombinant) 10009818

NF-κB1, Nuclear Factor-κB (p50)
M_r: 74.5 kDa **Purity:** ≥75% **Stability:** ≥6 months at -80°C
Source: Recombinant GST-tagged protein expressed in *E. coli* • As part of a dimer, this transcription factors binds with p65 to form NF-κB, which is responsible for regulating the expression of inflammatory cytokines, chemokines, immunoreceptors, and cell adhesion molecules.

5 µg
10 µg
25 µg

PPARα LBD (human recombinant) 10009088

Peroxisome Proliferative Activated Receptor α, PPARα Ligand Binding Domain
M_r: ~34 kDa **Purity:** ≥90% **Stability:** ≥6 months at -80°C
Source: Recombinant His-tagged protein expressed in *E. coli* • PPARα transcriptionally regulates a variety of genes involved in fatty acid metabolism and oxidation, such as acyl-CoA oxidase, enol-CoA hydratase, medium chain fatty acyl-CoA dehydrogenase, fatty acid transport protein, and CYP450 4A isozymes. Cayman's PPARα LBD contains amino acids 170-430 from full length human PPARα.

25 µg
50 µg
100 µg

PPARδ (human recombinant) 10007451

FAAR, NUC1, Nuclear Hormone Receptor 1, Peroxisome Proliferative Activated Receptor δ, PPARβ
M_r: 54 kDa **Purity:** ≥95% **Stability:** ≥6 months at -80°C
Source: Recombinant protein expressed in *Sf*21 cells • PPARs are members of the nuclear receptor family of ligand activated transcription factors that heterodimerize with retinoic acid like receptors, regulating gene expression and differentiation. PPARδ is a mediator of diverse physiological functions including lipid and cholesterol homeostasis, embryo implantation, and cancer development. Most recently, attention has been focused on the role of PPARδ in obesity.

10 µg
25 µg
50 µg

PPARδ Western Ready Control 10009568

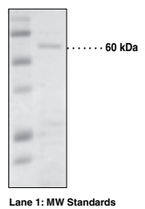
FAAR, NUC1, Nuclear Hormone Receptor 1, Peroxisome Proliferative Activated Receptor δ ,PPARβ
Purity: Whole cell lysate **Stability:** ≥2 years at -20°C
Source: Human recombinant N-terminal His-tagged protein expressed in *Sf*21 cells • Application(s): Positive control for WB • PPARδ is a mediator of diverse physiological functions including lipid and cholesterol homeostasis, embryo implantation, and cancer development. Most recently, attention has been focused on the role of PPARδ in obesity.

1 ea

PPARγ FL (human recombinant from *E. coli*) 61700

Peroxisome Proliferative Activated Receptor γ, PPARγ Full Length
M_r: 60 kDa **Purity:** ≥90% **Stability:** ≥6 months at -80°C
Source: Recombinant N-terminal His-tagged protein expressed in *E. coli* • PPARs are members of the nuclear receptor family of ligand activated transcription factors that heterodimerize with retinoic acid like receptors, regulating gene expression and differentiation. PPARγ has been implicated in the pathology of numerous diseases including obesity, diabetes, atherosclerosis, and cancer.

5 µg
10 µg
25 µg
50 µg

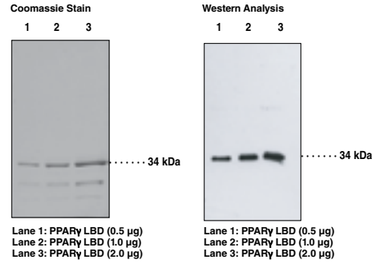


Lane 1: MW Standards
Lane 2: PPARγ FL (2 µg)

PPARγ LBD (human recombinant) 10007941

Peroxisome Proliferator Activated Receptor γ Ligand Binding Domain, PPARγ Ligand Binding Domain
M_r: ~34 kDa **Purity:** ≥90% **Stability:** ≥6 months at -80°C
Source: Recombinant N-terminal His-tagged protein expressed in *E. coli* • PPARγ has been implicated in the pathology of numerous diseases including obesity, diabetes, atherosclerosis, and cancer. Binding of activating ligands to the LBD promotes heterodimerization with retinoic acid-like receptor (RXR) resulting in the regulated expression of target genes, a significant number of which are related to lipid metabolism.

25 µg
50 µg
100 µg



Lane 1: PPARγ LBD (0.5 µg)
Lane 2: PPARγ LBD (1.0 µg)
Lane 3: PPARγ LBD (2.0 µg)

Lane 1: PPARγ LBD (0.5 µg)
Lane 2: PPARγ LBD (1.0 µg)
Lane 3: PPARγ LBD (2.0 µg)

Protein Phosphatase 2A C subunit (human recombinant; L309 deletion) 10011237

PP2A Cα, PP2A L309, PP2A A^{309}
M_r: 38.6 kDa **Purity:** ≥90% **Stability:** ≥6 months at -80°C
Source: Active recombinant PP2A catalytic subunit expressed in *Sf*21 cells with an N-terminal octahistidine-tag followed by a streptactin-tag; C-terminal leucine 309 was deleted • PP2A is a divalent cation-independent protein serine/threonine phosphatase involved in regulating numerous cellular processes including the cell cycle, growth, and differentiation and is also thought to be a potential tumor suppressor.

5 µg
10 µg
50 µg

Protein Tyrosine Phosphatase 1B (human recombinant) 10010896

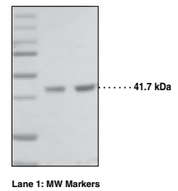
PTP1B
M_r: 37.3 kDa **Purity:** ≥95% **Stability:** ≥6 months at -80°C
Source: Active recombinant protein expressed in *E. coli* • PTPs remove phosphate from tyrosine residues of cellular proteins. Reversible phosphorylation catalyzed by the coordinated actions of protein tyrosine kinases and phosphatases is of paramount importance to the regulation of the signaling events that underlie such fundamental processes as growth and proliferation, differentiation, and survival or apoptosis, as well as adhesion and motility. One of the most heavily studied PTP proteins is PTP1B.

25 µg
50 µg
100 µg

PtdIns-(3,4,5)-P_3 Binding Protein 10009817

GRP1 PH Domain, PI(3,4,5)-P_3, PIP_3
M_r: 41.7 kDa **Purity:** ≥95% **Stability:** ≥1 year at -80°C
Source: Human recombinant N-terminal GST-tagged protein expressed in *E. coli* • PtdIns-(3,4,5)-P_3 binding protein contains a highly specific PH domain that recognizes and binds PtdIns-(3,4,5)-P_3. PtdIns phosphates play a critical role in the generation and transmission of cellular signals. Due to PtdIns-(3,4,5)-P_3 binding protein's unique affinity for PtdIns-(3,4,5)-P_3, this protein can be used to detect product formed by PI3-kinase in *in vitro* assays.

25 µg
50 µg
100 µg

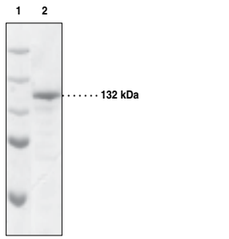


Lane 1: MW Markers
Lane 2: PtdIns-(3,4,5)-P_3 (1 µg)
Lane 3: PtdIns-(3,4,5)-P_3 (2 µg)

PtdIns-(4)-P_1 Binding Protein 10009241

PI(4)-P_1, PIP, SidC, SidC 3C
M_r: 132 kDa **Purity:** ≥90% **Stability:** ≥1 year at -80°C
Source: Human recombinant N-terminal GST-tagged protein expressed in *E. coli* • PtdIns-(4)-P_1 binding protein contains a highly specific PH domain that recognizes and binds PtdIns-(4)-P_1. PtdIns-(4)-P_1 can be phosphorylated by kinases to give bi- and triphosphates such as PtdIns-(4,5)-P_2 and PtdIns-(3,4,5)-P_3 to initiate an intricate signaling cascade that has been implicated in cancer.

25 µg
50 µg
100 µg

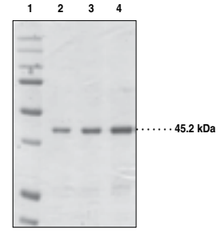


Lane 1: MW Markers
Lane 2: PtdIns-(4)-P_1 Binding Protein (1.25 µg)

PtdIns-(4,5)-P_2 Binding Protein 10009815

PI(4,5)-P_2, PIP_2, PLC-δ1-PH Domain
M_r: 45.2 kDa **Purity:** ≥95% **Stability:** ≥1 year at -80°C
Source: Human recombinant N-terminal GST-tagged protein expressed in *E. coli* • PtdIns-(4,5)-P_2 binding protein contains a highly specific PH domain that recognizes and binds PtdIns-(4,5)-P_2. PtdIns-(4,5)-P_2 can be phosphorylated by phosphoinositide (PI)-3-kinase to make PtdIns-(3,4,5)-P_3 which initiates an intricate signaling cascade that has been implicated in cancer. PtdIns-(4,5)-P_2 binding protein can be used in *in vitro* assays for the detection of PtdIns-(4,5)-P_2 in PI3-kinase and PTEN phosphatase assays.

25 µg
50 µg
100 µg



Lane 1: MW Markers
Lane 2: PtdIns-(4,5)-P_2 (0.5 µg)
Lane 3: PtdIns-(4,5)-P_2 (1.0 µg)
Lane 4: PtdIns-(4,5)-P_2 (2.0 µg)

PTEN (human recombinant) 10009746

MMAC1, Phosphatidylinositol 3-phosphatase, TEP1
M_r: 50.8 kDa **Purity:** ≥95% **Stability:** ≥6 months at -80°C
Source: Active recombinant N-terminal His-tagged protein expressed in *Sf*21 cells • PTEN functions as a key regulatory enzyme in many signal transduction pathways by dephosphorylating proteins and lipids such as Akt and PIP_3. Mutation of PTEN results in many human cancers including melanoma and prostate carcinoma, making PTEN an important tumor suppressor.

25 µg
50 µg
100 µg

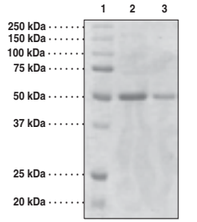
Sphingosine Kinase 1 (human recombinant) 10348

SK1, SPHK 1

M_r: 47.5 kDa **Purity:** ≥90% **Stability:** ≥6 months at -80°C

Source: Active recombinant N-terminal His-tagged protein from *Sf*9 cells • SPHK 1 catalyzes the production of sphingosine-1-phosphate, a lipid mediator with broad spectrum of biological activities including cell proliferation, survival, migration, cytoskeletal organization, and morphogenesis.

10 µg
25 µg
50 µg



Lane 1: MW Markers
Lane 2: SPHK1 (5 µg)
Lane 3: SPHK1 (2.5 µg)

Sphingosine Kinase 2 (human recombinant) 10009237

SK2, SPHK 2

M_r: 69.5 kDa **Purity:** ≥80% **Stability:** ≥6 months at -80°C

Source: Active recombinant N-terminal His-tagged protein expressed in *Sf*9 cells • SPHK 2 catalyzes the phosphorylation of sphingosine to S1P. SPHK 2 is a potential therapeutic target for the control of cancer, inflammation, and other diseases.

1 ea

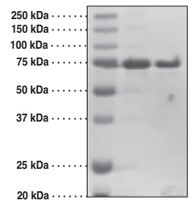
TNF Receptor-Associated Protein 1 (human recombinant) 11105

Hsp75, Hsp90L, Mitochondrial Heat Shock Protein 75 kDa, TRAP1

M_r: 76.3 kDa **Purity:** ≥95% **Stability:** ≥1 year at -80°C

Source: Recombinant C-terminal FLAG-tagged protein expressed in *E. coli* • TRAP1 is a mitochondrial protein that plays a role in maintaining mitochondrial function and regulating cell apoptosis as a pro-survival protein.

5 µg
10 µg
25 µg



Lane 1: MW Markers
Lane 2: TRAP1 (4 µg)
Lane 3: TRAP1 (2 µg)

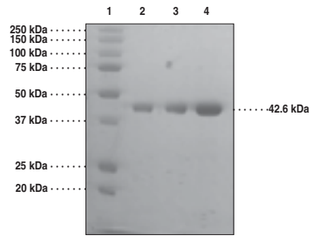
TP53BP1 tudor-like region (human recombinant) 14073

53BP1, Tumor Suppressor p53-binding Protein 1

M_r: 42.6 kDa **Purity:** ≥90% **Stability:** ≥6 months at -80°C

Source: Recombinant N-terminal GST-tagged protein expressed in *E. coli* • This product contains the tudor domain of TP53BP1. Binding of TP53BP1 to dimethylated lysine 382 on p53 (p53 K382me2), as well as histone H4K20me2, through the tudor domain, has been shown to be important for TP53BP1 localization to DNA double strand breaks.

25 µg
50 µg
100 µg



Lane 1: MW Markers
Lane 2: TP53BP1 (1 µg)
Lane 3: TP53BP1 (2 µg)
Lane 4: TP53BP1 (5 µg)

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Abbreviations

Aβ	Amyloid Beta
AhR	Aryl hydrocarbon Receptor
AIF	Apoptosis-Inducing Factor
AMP	Adenosine Monophosphate
AMPK	AMP-activated Protein Kinase
Apaf	Apoptosis Protease-Activating Factor
ARE	Antioxidant Response Element
ATP	Adenosine Triphosphate
CaMK	Calcium/Calmodulin-dependent Protein Kinase
cAMP	Adenosine 3',5'-cyclic monophosphate
CARD	Caspase Recruitment Domain
Cdc	Cell division cycle
CDK	Cyclin-dependent Kinase
cGMP	Guanosine 3',5'-cyclic monophosphate
ChIP	Chromatin Immunoprecipitation
CK	Casein Kinase
CoA	Coenzyme A
COX	Cyclooxygenase
CREB	cAMP Response Element-binding Protein
CXCR	Alpha Chemokine Receptor
CYP	Cytochrome
CysLT	Cysteinyl Leukotriene
DNA	Deoxyribonucleic Acid
EC_{50}	Half maximal effective concentration
EGFR	Epidermal Growth Factor Receptor
EIA	Enzyme Immunoassay
ELISA	Enzyme-linked Immunosorbent Assay
ER	Estrogen Receptor
ERK	Extracellular Signal-Related Kinase
FADD	Fas-Associated Protein with Death Domain
FC	Flow Cytometry
FITC	Fluorescein Isothiocyanate
FP	Fluorescence Polarization
FTase	Farnesyltransferase
FXR	Farnesoid X Receptor
GEF	Guanine Nucleotide Exchange Factor
GI_{50}	Growth Inhibition
GMP	Guanosine Monophosphate
GPCR	G Protein-Coupled Receptor
GSK	Glycogen Synthase Kinase
GST	Glutathione S-Transferase
GTP	Guanosine Triphosphate
HAT	Histone Acetyltransferase
HDAC	Histone Deacetylase
HER2	Human Epidermal Growth Factor Receptor 2
HIF	Hypoxia Inducible Factor
HIV	Human Immunodeficiency Virus
HNF4α	Hepatocyte Nuclear Factor 4α
HRP	Horseradish Peroxidase
HSP	Heat Shock Protein
IC_{50}	Half maximal inhibitory concentration
ICC	Immunocytochemistry
IF	Immunofluorescence
IHC	Immunohistochemistry
IκB-α	Nuclear Factor κ-light-chain-enhancer of activated B cells Inhibitor-α
IKK	IκB Kinase
IL	Interleukin
iNOS	Inducible Nitric Oxide Synthase
IP	Immunoprecipitation
IP_3	Inositol Triphosphate
IPF	Idiopathic Pulmonary Fibrosis
JAK	Janus Kinase
JMJD	Jumonji-domain
K_d	Dissociation Constant
K_i	Inhibition Constant
LDL	Low-Density Lipoprotein
LO	Lipoxygenase
LPS	Lipopolysaccharide
LT	Leukotriene
LXR	Liver X Receptor
MAPK	Mitogen-activated Protein Kinase
MLCK	Myosin Light-Chain Kinase
mTOR	Mammalian Target of Rapamycin
NAD	Nicotinamide Adenine Dinucleotide
NFAT	Nuclear Factor of Activated T cells
NF-κB	Nuclear Factor κ-light-chain-enhancer of activated B cells
NO	Nitric Oxide
NOD1	Nucleotide-binding Oligomerization Domain-containing Protein 1
NOS	Nitric Oxide Synthase
PARP	Poly(ADP-ribose) polymerase
pCAF	p300/CBP-associated factor
PDE	Phosphodiesterase
PDGFR	Platelet-derived Growth Factor Receptor
PDK1	3-Phosphoinositide-dependent Protein Kinase-1
PGE	Prostaglandin E
PGES	Prostaglandin E Synthase
PHD	Prolyl Hydroxylase Domain
PI	Phosphoinositide
PK	Protein Kinase
PL	Phospholipase
PMA	Phorbol Myristate Acetate
PP	Protein Phosphatase
PPAR	Peroxisome Proliferator-activated Receptor
PRK	p53-Regulating Kinase
PtdIns	Phosphatidylinositols
PTEN	Phosphatase and Tensin Homolog
PTP	Protein Tyrosine Phosphatase
RAGE	Receptor for Advanced Glycation Endproducts
RAR	Retinoic Acid Receptor
Ras	Rat sarcoma
Ret	Rearranged during transfection
RNA	Ribonucleic Acid
ROCK	Rho-associated Protein Kinase
ROS	Reactive Oxygen Species
RXR	Retinoid X Receptor
sEH	Soluble Epoxide Hydrolase
SERCA	Sarco/Endoplasmic Reticulum Calcium-ATPase
SERM	Selective Estrogen Receptor Modulator
S1P	Sphingosine-1-Phosphate
SPHK	Sphingosine Kinase
SREBP	Sterol Regulatory Element-Binding Protein
SRF	Serum Response Factor
STAT	Signal Transducer and Activator of Transcription
TGF	Transforming Growth Factor
TLR4	Toll-like Receptor 4
TNF	Tumor Necrosis Factor
TNFR	Tumor Necrosis Factor Receptor
TRADD	Tumor Necrosis Factor Receptor Type 1-Associated Death Domain Protein
Tregs	Regulatory T cells
VEGF	Vascular Endothelial Growth Factor
WB	Western Blot
XIAP	X-linked Inhibitor of Apoptosis Protein

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