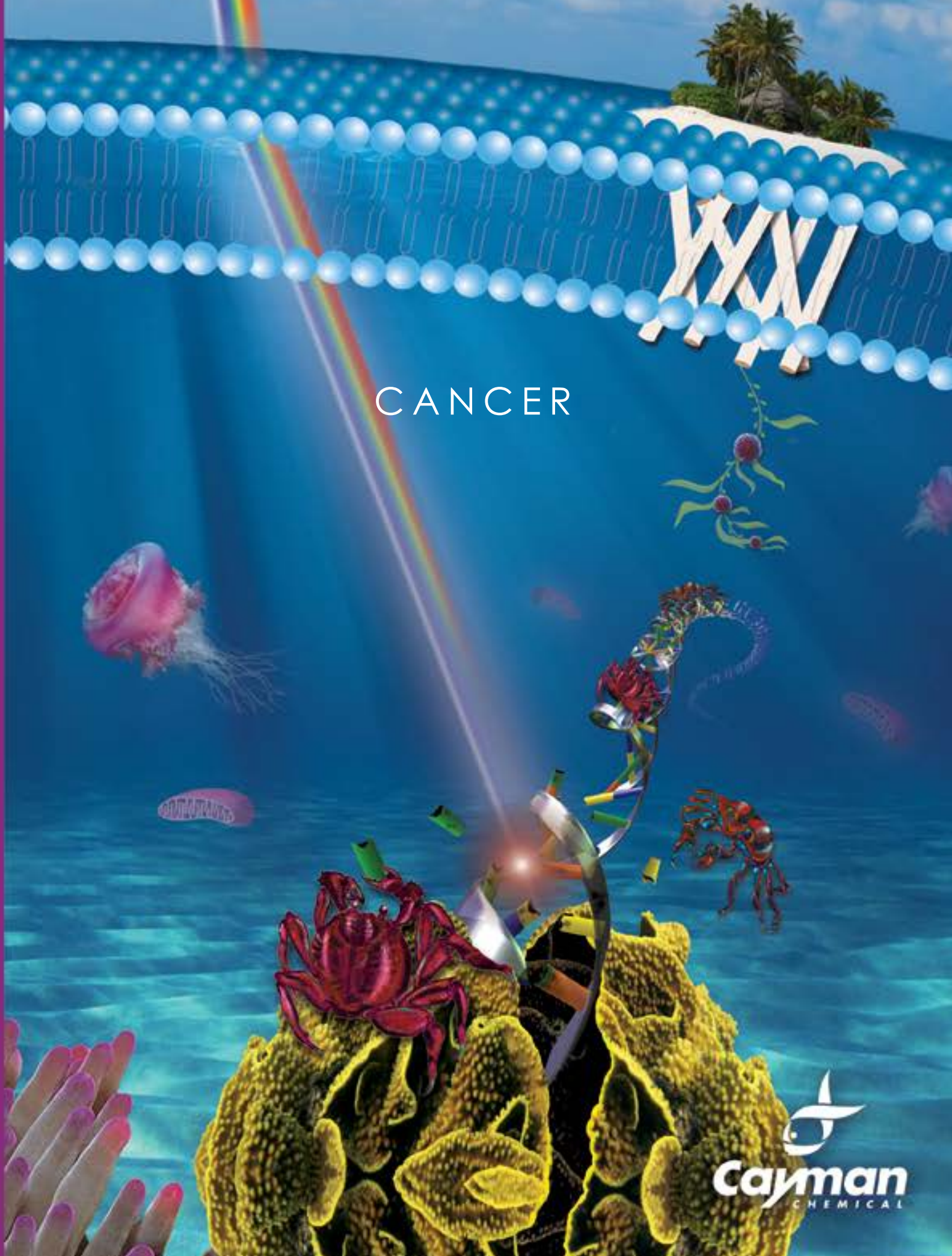
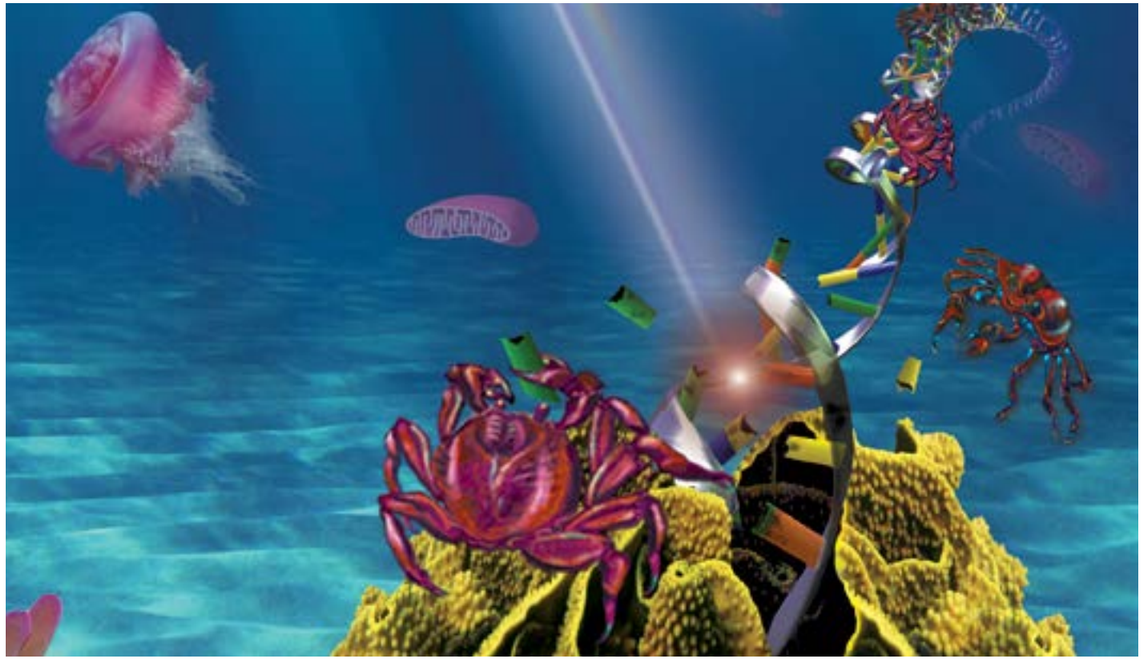

XXI
CANCER
Cayman
CHEMICAL

Thomas G. Brock, Ph.D.

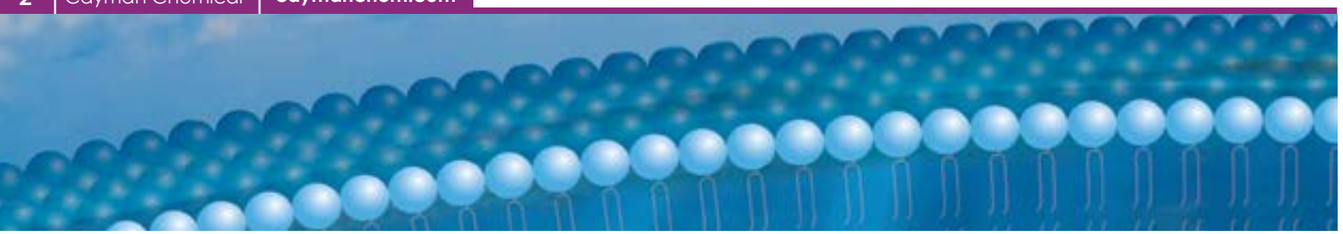
Introduction to Cancer



Radiation. Cancer. The emotional impact of these two words is immediate and dreadful for most people, and almost equally so. But radiation is essential to human health – so that as humans migrated northwards over the eons, evolution disabled the melanin shield in their skin to enable the life-giving UV light adequate penetration. But those same photons wreak havoc on our fragile strands of DNA, as illustrated in the cellular seascape on our cover. DNA-repair enzymes rush to the rescue, suggested by the crabs swarming to the nucleus. But when that repair fails, cancer often makes its appearance.

Unfortunately, prevention of cancer can never be as simple as fearful avoidance of sunlight and radiation. Cayman scientists have worked with the cancer researchers and doctors at the nearby University of Michigan, and our experience is that cancer causation is multifactorial and complicated. Cancer patients arrive every day of the year. They come from every ethnic group and economic class, from the young and the old. Cancer is so pervasive that almost every one of us knows a friend, a relative, perhaps a co-worker, who has cancer or perhaps had cancer. And, as cancer survivors know in a very personal and intimate way, the shadow of the disease lingers long after treatment has finished.

Cancer is the topic of this catalog and our purpose is to assist in research efforts to find cures for the varied forms of cancer. This catalog brings to the research community the best that Cayman offers toward the pursuit of fighting each of the many types of cancers. In addition, there are informative articles that are relevant to cancer, including the epigenetics of EZH2. Most importantly, this catalog serves as a bridge between you, the researcher, and Cayman. Cayman is an interactive company. We listen and respond positively to your requests for new compounds and products. Cayman also offers its expertise and facilities to you through our Contract Services, where we analyze your samples, run your samples in our assays, and perform custom chemical syntheses. Take a look at our website, caymanchem.com, or call us to find out how we can work together in the fight against cancer.



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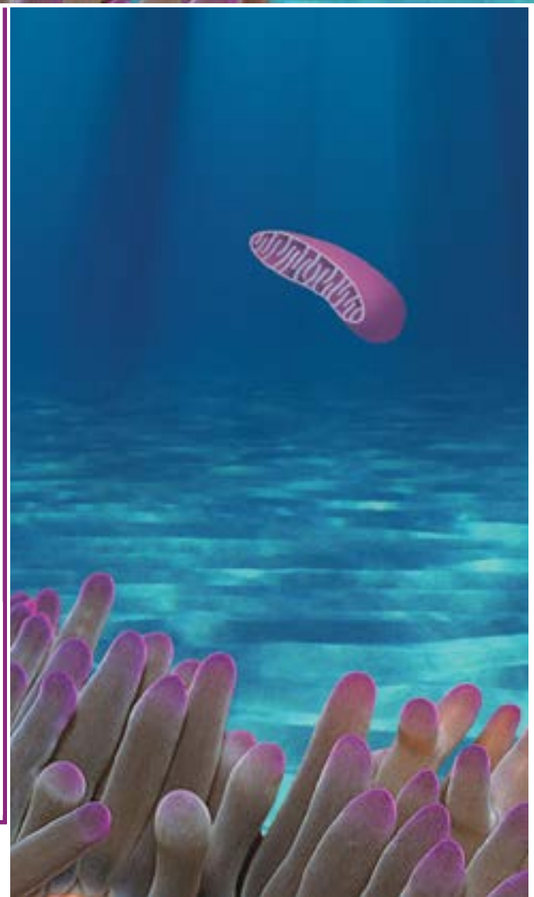
Cn

CANCER



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abbrevia-

ADHP	10-Acetyl-3, 7-Dihydroxyphenoxazine
ADP	Adenosine Diphosphate
ATP	Adenosine Triphosphate
Cdk	Cyclin-Dependent Kinase
CK	Casein Kinase
COX	Cyclooxygenase
CREB	cAMP Response Element Binding Protein
CYP	Cytochrome P
DNA	Deoxyribonucleic Acid
EGFR	Epidermal Growth Factor Receptor
EIA	Enzyme Immunoassay
ELISA	Enzyme-Linked Immunosorbent Assay
EP	Prostaglandin E Receptor
ER	Estrogen Receptor Endoplasmic Reticulum
ERK	Extracellular Signal-Regulated Kinase
FC	Flow Cytometry
FITC	Fluorescein Isothiocyanate
FRET	Fluorescent Resonant Energy Transfer
GPCR	G Protein-Coupled Receptors
GSK	Glycogen Synthase Kinase
GST	Glutathione-S-Transferase
HAT	Histone Acetyltransferase
HDAC	Histone Deacetylases
HIF	Hypoxia Inducible Factor
His	Hexahistidine
HMT	Histone methyltransferases
Hsp	Heat-Shock Protein
ICC	Immunocytochemistry
IF	Immunofluorescence
IHC	Immunohistochemistry
IL	Interleukin
IP	Immunoprecipitation
KLH	Keyhole Limpet Hemocyanin
LO	Lipoxygenase
LPA	Lysophosphatidic Acid
LPS	Lipopolysaccharide
LSD	Lysine-Specific Demethylase
MAPK	Mitogen Activated Protein Kinase
MBD	Methyl binding domain
MMP	Matrix Metalloproteinase
PBS	Phosphate Buffered Saline
PE	Phycoerythrin
PG	Prostaglandin
PGES	Prostaglandin E Synthase
PI3K	Phosphoinositide 3-Kinase
PL	Phospholipase
PP	Protein Phosphatase
PRMT	Protein Arginine Methyltransferases
RTK	Receptor tyrosine kinases
SAMe	S-Adenosyl-L-Methionine
SIP	Sphingosine-1-Phosphate
SIRT	Silent Information Regulator
SPHK	Sphingosine Kinase
TNF-α	Tumor Necrosis Factor-α
TP	Thromboxane Receptor
TX	Thromboxane
VEGF	Vascular Endothelial Growth Factor
WB	Western Blot

vol. 11 Cn

Thomas G. Brock, Ph.D.

PGE_2, COX-2, and mPGES-1 in Cancer

This one molecule does it all. Prostaglandin E_2 (PGE_2) causes relaxation of smooth muscle in the kidney but contraction of smooth muscle in the peripheral vessels and airway. It promotes bone formation and inhibits sleep, causes fever and suppresses leukocyte function. PGE_2 is well known to induce fever and pain, but protects the gastrointestinal system by promoting duodenal bicarbonate secretion and inhibiting gastric acid production. It regulates circadian rhythms and inhibits lipolysis. PGE_2 is essential for ovarian follicle growth, promotes cervical relaxation and causes uterine contraction. Neonatal exposure to PGE_2 promotes masculinization in rat pups, whereas blocking PGE_2 leads to more female-like behaviors. The effects of PGE_2 are so diverse that, perhaps, it's not surprising that it's involved in a host of diseases.

In general terms, PGE_2 is best known as a pro-inflammatory mediator: it is over-produced at sites of inflammation, and it causes two cardinal characteristics of inflammation: pain and fever. It's likely that every person reading this article is familiar with over-the-counter pain treatments, although few may be aware that the primary target of non-steroidal anti-inflammatory drugs (NSAIDs) is PG production. More relevant to this catalog, PGE_2 may be involved in many types of cancer, including bladder, breast, cervical, colorectal, esophageal, head and neck, skin, lung, oral, and prostate cancers, as well as multiple myeloma. At first thought, it may seem reasonable that PGE_2 is linked with inflammatory aspects of these cancers and contributes to pain related to the disease. However, bear in mind that PGE_2 can do much more than cause pain. This article examines the sources of PGE_2 and its value as a biomarker in certain cancers.

The Sources of PGE_2

PGE_2 is a lipid mediator. As such, it can be distinguished from protein mediators (cytokines) on many levels. Lipid mediators are produced enzymatically from readily available precursors, so their levels can rise rapidly (in a matter of minutes), while cytokine synthesis is slower, involving transcription and translation. On the other hand, the continuous, low level production of PGE_2 is important in both normal and pathological circumstances. Lipid mediators can also be rapidly eliminated, through both enzymatic and non-enzymatic pathways. Related to this, the actions of lipid mediators like PGE_2 are local, affecting the source cell (described as 'autocrine' effects) or neighboring cells ('paracrine' actions). Remarkably, many lipid mediators, including PGE_2, act through specific receptors, much like cytokines.

The synthesis of PGs from arachidonic acid is initiated by the cyclooxygenases, COX-1 and COX-2 (Figure 1). Both enzymes are membrane-bound homodimers, found predominantly on the perinuclear membranes, including the endoplasmic reticulum. COX-1 is commonly described as ubiquitous and constitutively expressed. COX-2, on the other hand, is normally absent from most cell types, its expression is induced by inflammatory mediators like TNF-α and IL-1β, and both its mRNA and protein have short half-lives. NSAIDs, including aspirin, ibuprofen, and indomethacin, non-selectively inhibit both COX-1 and COX-2, blocking the synthesis of all PGs. The overuse of NSAIDs can lead to damage in the gastrointestinal and renal systems through its inhibition of COX-1 (PGs have protective effects in these systems). This supports a generalization that COX-1 is 'good', producing products that are needed to maintain health and homeostasis, while COX-2 is 'bad'. Surprisingly, COX-2-selective NSAIDS, including celecoxib and rofecoxib, while effectively suppressing pain, have unwanted side effects, particularly in the cardiovascular system. Thus, even COX-2 has its good side.

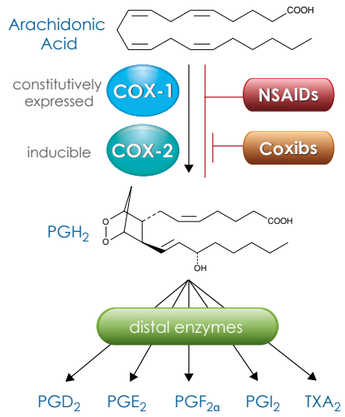

Figure 1. COX-1 and COX-2 convert arachidonic acid to the intermediate PGH_2, which is then metabolized by specific distal enzymes to produce the different PGs and thromboxane. NSAIDs inhibit both COX forms, while the coxibs selectively inhibit COX-2.

In cancer, COX-2 is clearly bad. It appears to be over-expressed in many types of cancer, including colorectal, breast, prostate, lung, stomach, and esophageal cancers. Some of the most compelling data relates to individuals with familial adenomatous polyposis (FAP). In the classic form of this inherited disorder, benign growths (polyps) begin to appear in the colon during the teen years and increase in number throughout the next two decades. Some of these adenomas eventually transition into dysplasia, inevitably progressing to carcinoma in middle-aged adults. In both human FAP and murine models of the disease, COX-2 is constitutively over-expressed in the colon. Treatment with NSAIDs prevents tumor formation in mouse models of FAP.[1] More importantly, NSAIDs can produce a regression of intestinal adenomas and prevent colorectal cancer in humans.[2] These and numerous other studies have demonstrated that NSAIDs are chemopreventive in colorectal cancer. A recent international consensus statement reports that aspirin, because of its known cardiovascular benefit and available safety and efficacy data, is the 'most likely' NSAID for use in chemoprevention.[3] In this report, other NSAIDs, either selective or non-selective for COX-2, were dismissed because they do not provide cardioprotection. In fact, COX-2 selective NSAIDs carry a documented risk of adverse cardiovascular effects, which argue against their persistent use as chemopreventive drugs.[4] These problems may be attributed, at least in part, to cardioprotective effects of COX-2 products other than PGE_2, such as prostacyclin.[5]

The two COX enzymes produce only PG precursors (*e.g.*, PGH_2); the synthesis of PGE_2 is completed by PGE synthases (PGES), of which three distinct human gene products are known. The first, microsomal PGES-1 (mPGES-1), is a membrane-associated protein, like COX-1 and COX-2.[6] A 17.1 kDa protein that forms a homotrimer, it is highly expressed in human placenta, testis, small intestine, and colon, as well as in A549 cells (from a lung tumor) and HeLa cells (from cervical cancer). The expression of mPGES-1, like that of COX-2, is strongly and transiently induced by inflammatory mediators, giving rise to the paradigm that COX-2 and mPGES-1 are functionally coupled.[6] A second enzyme, mPGES-2, is synthesized at the Golgi membrane, then cleaved to produce the mature, cytosolic enzyme. It is constitutively expressed in many normal tissues and is not induced by inflammatory mediators. Mice deficient in this enzyme showed no change in PGE_2 production in several tests, raising the question of whether this enzyme is truly a PGE_2 synthase.[7] Finally, cytosolic PGES (cPGES) is also known as p23 and associates with numerous proteins, including heat shock proteins Hsp70 and Hsp90. These complexes bind to genomic response elements in a hormone-dependent manner. Over-expression of cPGES in cells suggests that this enzyme converts PGH_2 derived from COX-1, but not COX-2, to PGE_2, functionally linking cPGES with COX-1.[8]

The enzyme mPGES-1 is currently considered a key target for therapeutic intervention in many diseases, including cancer.[9,10] This enzyme is over-expressed in several types of cancer. Also, induced over-expression of mPGES-1 in experimental systems contributes to tumor growth, metastasis, angiogenesis, and resistance to apoptosis, whereas knockdown reverses these effects.[11-13] Thus, mPGES-1 appears, at this point, to be a better target for cancer treatment than COX-2. Certainly the inhibition of mPGES-1 is a more specific way to diminish PGE_2 synthesis.

PGE_2 Metabolites as Biomarkers

The COX enzymes initiate the synthesis of numerous products, including PGE_2, prostacyclin (PGI_2), thromboxane (TXA_2), PGD_2, and $PGF_{2\alpha}$. Each of these activates one or more selective GPCRs which are distributed on specific types of cells to generate distinctive physiological responses. For example, PGE_2 activates four 'E prostanoid' receptors, $EP_{1\text{-}4}$, and these activate different intracellular signaling pathways to alter cell function (described in detail in a related article on page 12). An overview of PGE_2 signaling is provided in Figure 2.

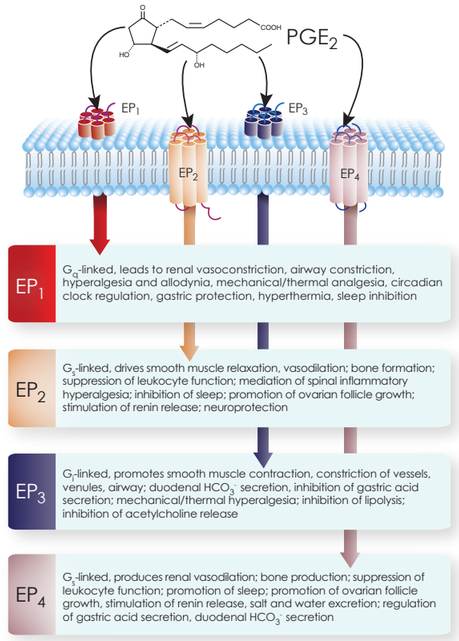

Figure 2. The four 'E prostanoid' (EP) receptors evoke distinct effects, in part due to differences in intracellular signaling.

Of all the COX products, it is primarily PGE_2 that has been associated with contributing to cancer. Interestingly, the induced expression of COX-2 does not simply lead to an increase in all COX products but tends to drive a selective overproduction of PGE_2.[14] This is due, at least in part, to the concomitant increased expression of mPGES-1 with COX-2. In addition, PGE_2 feeds back to positively increase COX-2 expression, further augmenting its own synthesis. In the microenvironment of the tumor, this creates a vicious cycle where tumor-related signaling increases COX-2 expression leading to PGE_2 production, which not only drives angiogenesis while suppressing apoptosis and innate immunity but also heightens COX-2 expression and perpetuates PGE_2 synthesis.

As mentioned above, PGE_2 acts in a very localized fashion and is rapidly metabolized. In serum and tissues, PGE_2 is rapidly metabolized to 15-keto PGE_2 by 15-hydroxy PG dehydrogenase (15-PGDH), an enzyme which can metabolize a variety of PGs in an NAD^+-dependent fashion (Figure 3). 15-keto PGE_2 is further altered by additional enzymatic and non-enzymatic processes to produce 13,14-dihydro-15-keto-PGE_2 and tetranor PGEM. Reduced expression of 15-PGDH leads to prolonged availability and action of PGE_2 and has been linked to several cancers, including colorectal, bladder, pancreatic, and gastric adenocarcinomas.[15-18] On the other hand, the expression of 15-PGDH is significantly increased in ovarian cancer.[19]

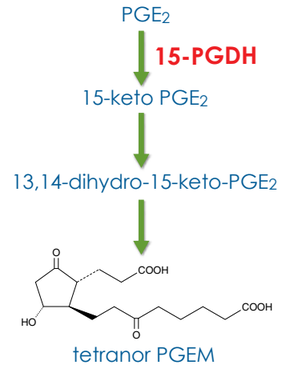

Figure 3. 15-PGDH is the gatekeeper of PGE_2 metabolism. Reduced 15-PGDH activity has been linked to several cancers.

There are two approaches to monitoring PGE_2 production in the context of cancer. First, PGE_2 itself can be measured in the media of cells studied in culture, since 15-PGDH, the critical enzyme for metabolizing PGE_2, is usually not produced by cells in culture. It may also be appropriate to measure PGE_2 in cancerous tissues, particularly when the level of 15-PGDH is expected to be suppressed. However, measuring the levels of PGE_2 metabolites in urine, such as 13,14-dihydro-15-keto-PGE_2, provides an indirect and non-invasive way to evaluate PGE_2 synthesis in the body as a whole. This approach has been used to demonstrate the increased synthesis of PGE_2 in individuals with colorectal and lung cancer.[20-22]

Cayman Chemical is a world leader in the analysis of PGs and their pathway enzymes. In the pages of this catalog, you will find many of the reagents, antibodies, and assays that we have available for research. For further information and additional products, please visit us at caymanchem.com.

References

1. Boolbol, S.K., Dannenberg, A.J., Chadburn, A., *et al. Cancer Res.* **56**, 2556-2560 (1996).
2. Iwama, T. *J. Gastroenterol.* **44[Suppl XIX]**, 72-76 (2009).
3. Cuzick, J., Otto, F., Baron, J.A., *et al. Lancet Oncol.* **10**, 501-507 (2009).
4. Friedewald, V.E., Bennett, J.S., Christo, J.P., *et al. Am. J. Cardiol.* **106**, 873-884 (2010).
5. Capone, M.L., Tacconelli, S., Rodriguez, L.G., *et al. Pharmacol. Rep.* **62**, 530-535 (2010).
6. Jakobsson, P-J., Thorén, S., Morgenstern, R., *et al. Proc. Natl. Acad. Sci. USA* **96**, 7220-7225 (1999).
7. Jania, L.A., Chandrasekharan, S., Backlund, M.G., *et al. Prostaglandins Other Lipid Mediat.* **88**, 73-81 (2009).
8. Tanioka, T., Nakatani, Y., Semmyo, N., *et al. J. Biol. Chem.* **275**, 32775-32782 (2000).
9. Hara, S., Kamei, D., Sasaki, Y., *et al. Biochimie* **92**, 651-659 (2010).
10. Nakanishi, M., Gokhale, V., Meuillet, E.J., *et al. Biochimie* **92**, 660-664 (2010).
11. Kamei, D., Murakami, M., Sasaki, Y., *et al. Biochem. J.* **425**, 361-371 (2010).
12. Hanaka, H., Pawelzik, S.-C., Johnsen, J.I., *et al. Proc. Natl. Acad. Sci. USA* **106(44)**, 18757-18762 (2009).
13. Kamata, H., Hosono, K., Suzuki, T., *et al. Biomed. Pharmacother.* **64**, 409-416 (2010).
14. Brock, T.G., McNish, R.W., and Peters-Golden, M. *J. Biol. Chem.* **274**, 11660-11666 (1999).
15. Lim, S.C., Cho, H., Lee, T.B., *et al. Yonsei Med. J.* **51(5)**, 692-699 (2010).
16. Tseng-Rogenski, S., Gee, J., Ignatoski, K.W., *et al. Am. J. Pathol.* **176(3)**, 1462-1468 (2010).
17. Pham, H., Chen, M., Li, A., *et al. Pancreas* **39(3)**, 332-339 (2010).
18. Tatsuwaki, H., Tanigawa, T., Watanabe, T., *et al. Cancer Sci.* **101(2)**, 550-558 (2010).
19. Thill, M., Fischer, D., Kelling, K., *et al. J. Steroid Biochem. Mol. Biol.* **121**, 387-390 (2010).
20. Murphey, L.J., Williams, M.K., Sanchez, S.C., *et al. Anal. Biochem.* **334**, 266-275 (2004).
21. Cai, Q., Gao, Y.-T., Chow, W.-H., *et al. J. Clin. Oncol.* **24(31)**, 5010-5016 (2006).
22. Murff, H.J., Shu, X.-O., Li, H., *et al. Cancer Epidemiol. Biomarkers Prev.* **18(8)**, 2283-2291 (2009).

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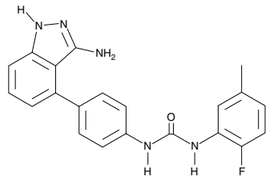
Stability: ≥1 year at 4°C
Summary: 7-AAD is a fluorescent dye which is excluded from live cells but penetrates dead or damaged cells to label DNA. Although 7-AAD fluorescence is less intense than that of propidium iodide, it exhibits a higher wavelength emission maximum (excitation at 488 nm, emission at 650 nm) and thus has minimal spectral overlap with PE or FITC. This makes 7-AAD preferable as a viability marker when FITC and/or PE are used simultaneously to label surface or intracellular antigens.

1 ea

ABT-869 13653

[796967-16-3] Linifanib
MF: $C_{21}H_{18}FN_5O$ **FW:** 375.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An ATP-competitive, multi-targeted RTK inhibitor that inhibits all members of the VEGF and PDGF receptor families (IC_{50}s = 4-190 nM); inhibits proliferation of MV-4-11 and MOLM-13 cells (IC_{50}s = 4 and 6 nM, recepectively)

1 mg
5 mg
10 mg
50 mg

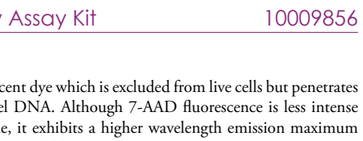


N-[4-(3-amino-1H-indazol-4-yl)phenyl]-N'-(2-fluoro-5-methylphenyl)-urea

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

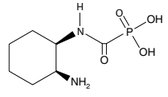


N-acetyl-L-α-aspartyl-L-α-glutamyl-N-(2-carboxyl-1-formylethyl)-L-valinamide

cis-ACCP 10012583

[777075-44-2]
MF: $C_7H_{15}N_2O_4P$ **FW:** 222.2 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A reversible and competitive inhibitor of type IV collagen-specific MMP-2 and MMP-9 with preference towards MMP-2 (IC_{50} = 4 and 20 µM, respectively)

1 mg
5 mg
10 mg
50 mg



P-[[[(1R,2S)-2-aminocyclohexyl]amino]carbonyl]-phosphonic acid

Acetyl Lysine Monoclonal Antibody (Clone 7F8) 10010567

Supplied as: Lyophilized IgG_1 **Stability:** ≥1 year at -20°C
Summary: Antigen: Acetylated KLH • Host: mouse • Cross Reactivity: (+) acetylated lysine residues; (-) non-acetylated lysine residues • Application(s): ELISA, ICC, and WB • Isotype: IgG_1 • This antibody is useful for monitoring levels of acetylation on various proteins (*e.g.,* histone and p53). Histone subunit modifications such as lysine acetylation are regulated by the activity of HATs and HDACs. Epigenetic modifications directly influence cellular genetic programs including those contributing to cancer cell viability. This monoclonal antibody was generated using acetylated KLH as an immunogen.

1 ea

Acetyl Lysine Polyclonal Antibody-biotin 13725

Supplied as: Rabbit immunoglobulin **Stability:** ≥1 year at -20°C
Summary: Antigen: acetylated KLH • Host: rabbit • Cross Reactivity: (+) acetylated lysine residues; (-) non-acetylated proteins • Application(s): ELISA, IF, IP, and WB • Reversible lysine acetylation and deacetylation play critical roles in regulating gene transcription, cell cycle progression, apoptosis, DNA repair, and cytoskeletal organization. This biotin-tagged antibody is useful for monitoring levels of acetylation on various proteins.

400 µl

Acetyl Lysine Polyclonal Antibody HRP Conjugate 13726

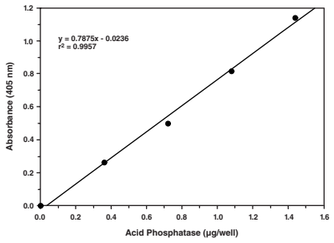
Supplied as: Rabbit immunoglobulin **Stability:** ≥1 year at -20°C
Summary: Antigen: acetylated KLH • Host: rabbit • Cross Reactivity: (+) • Application(s): ELISA, IF, IP, and WB • Reversible lysine acetylation and deacetylation play critical roles in regulating gene transcription, cell cycle progression, apoptosis, DNA repair, and cytoskeletal organization. This HRP-conjugated antibody is useful for monitoring levels of acetylation on various proteins.

400 µl

Acid Phosphatase Assay Kit 10008051

Stability: ≥6 months at 4°C
Summary: Cayman's Acid Phosphatase Assay provides a method for detecting AP activity in various matrices. The assay utilizes *para*-nitrophenyl phosphate (*p*NPP) as a chromogenic substrate for the enzyme. In the first step, AP dephosphorylates *p*NPP. In the second step, the phenolic OH-group is deprotonated under alkaline conditions resulting in *p*-nitrophenolate that yields an intense yellow color which can be measured at 405-414 nm.

480 wells



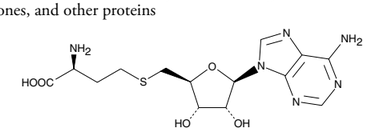
Akt Antibodies

Item No.	Item Name	Formulation	Host	Cross Reactivity	Application(s)
13733	Akt1 (Phospho-Ser^{473}) Monoclonal Antibody (Clone 104A282)	Protein G-purified IgG	Mouse, Clone 104A282	(+) Human and murine Akt1	IP and WB
13732	Akt1 Polyclonal Antibody	Protein G-purified IgG	Rabbit	(+) Human Akt1	WB
13734	Akt2 Monoclonal Antibody (Clone 95C567.1.2)	Ascites fluid	Mouse, Clone 95C567.1.2	(+) Human Akt2	WB
13735	Akt2/3 Polyclonal Antibody	Protein G-purified IgG	Rabbit	(+) Human Akt2/3	WB
13736	Akt3 Monoclonal Antibody (Clone 66C1247.1)	Protein G-purified IgG	Mouse, Clone 66C1247.1	(+) Human, murine, and rat Akt3	WB
13737	Akt3 Polyclonal Antibody	Protein G-purified IgG	Rabbit	(+) Human, murine, and rat Akt3	WB

S-Adenosylhomocysteine 13603

[979-92-0] AdoHcy, SAH
MF: $C_{14}H_{20}N_6O_5S$ **FW:** 384.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An amino acid derivative and an intermediate, by-product, or modulator of several metabolic pathways, including the activated methyl cycle and cysteine biosynthesis; also a product of SAM-dependent methylation of biological molecules, including DNA, RNA, histones, and other proteins

5 mg
10 mg
25 mg
50 mg



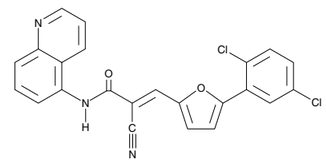
S-(5'-deoxyadenosin-5'-yl)-L-homocysteine

• Also Available: **S-Adenosylhomocysteine-d_4** (9000372) 500 µg, 1 mg, 5 mg, 10 mg

AGK2 13145

[304896-28-4]
MF: $C_{23}H_{13}Cl_2N_3O_2$ **FW:** 434.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A cell-permeable, selective inhibitor of SIRT2 (IC_{50} = 3.5 µM) that minimally affects either SIRT1 or SIRT3; rescues dopamine neurons from α-synuclein toxicity in both *in vitro* and *in vivo* Parkinson's disease models

1 mg
5 mg
10 mg
25 mg

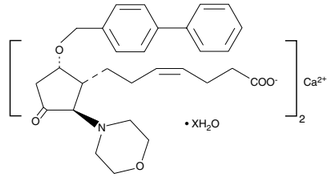


2-cyano-3-[5-(2,5-dichlorophenyl)-2-furanyl]-N-5-quinolinyl-2-propenamide

AH 23848 (calcium salt, hydrate) 19023

MF: $[C_{29}H_{34}NO_5]_2\ Ca^{2+} \bullet XH_2O$ **FW:** 1,011.3 **Purity:** ≥90%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A dual antagonist of TP and EP_4 receptors; inhibits TXA_2-induced platelet aggregation (IC_{50} = 0.26 µM) and bronchial smooth muscle contraction; impairs PGE_2-mediated relaxation of piglet saphenous vein, suppresses serum-induced proliferation of fibroblasts, and reduces metastasis in a murine model of breast cancer

1 mg
5 mg
10 mg
25 mg



7-[5α-([1S,1α(Z)-biphenyl]-4-ylmethoxy)-2β-(4-morpholinyl)-3-oxocyclopentyl]-4-heptenoic acid, calcium salt, hydrate

AIF Polyclonal Antibody 160773

Apoptosis-Inducing Factor, Programmed Cell Death Protein 8
Supplied as: 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 murine 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) 1 ea

Akt (human recombinant) Western Ready Control 10010079

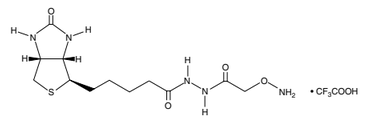
Akt1, PKB, Protein Kinase B
Stability: ≥2 years at -20°C
Summary: Source: human recombinant N-terminal His-tagged protein purified from *Sf*21 cells • Application(s): positive control for WB • M_r: 60.3 kDa (His-tagged), 57.3 (native)

1 ea

Aldehyde Reactive Probe (trifluoroacetate salt) 10009350

[627090-10-2] ARP, O-(Biotinylcarbazoylmethyl) Hydroxylamine
MF: $C_{12}H_{21}N_5O_4S \bullet C_2HF_3O_2$ **FW:** 445.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A biotinylated reagent used for the detection and quantification of apurinic/apyrimidinic (AP) sites in damaged DNA; reacts with aldehyde groups formed when reactive oxygen species depurinate DNA, thereby covalently linking biotin to these AP sites

5 mg
10 mg
25 mg
50 mg

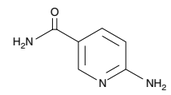


(6aR)-hexahydro-2-oxo-2-[(aminooxy)acetyl]hydrazide,1H-thieno[3aS,4S-d]imidazole-4-pentanoic acid, trifluoroacetate salt

6-Aminonicotinamide 10009315

[329-89-5] 6-AN, NSC 21206, SR 4388
MF: $C_6H_7N_3O$ **FW:** 137.1 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A well-established inhibitor of the $NADP^+$-dependent enzyme, 6-phosphogluconate dehydrogenase (K_i = 0.46 µM) which interferes with glycolysis; through ATP depletion, synergizes with chemotherapy drugs, like cisplatin, in killing cancer cells (IC_{50} = 0.5 mM); reduces cardiovascular oxidative injury following ischemia/reperfusion; causes glial neurodegeneration

100 mg
250 mg
500 mg
1 g

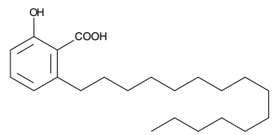


6-amino-3-pyridinecarboxamide

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 p300/CREB-binding protein-associated factor (pCAF) (IC_{50} = 8.5 and 5 µM, respectively); suppresses NF-κB activation, inhibits IκBα phosphorylation, and prohibits p65 nuclear translocation

5 mg
10 mg
25 mg
50 mg

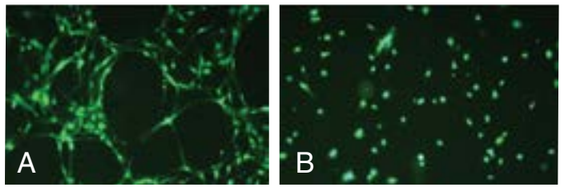


2-hydroxy-6-pentadecyl-benzoic acid

In Vitro Angiogenesis Assay Kit 10009964

Stability: ≥1 year at 4°C
Summary: Cayman's *In Vitro* Angiogenesis Assay uses a one-step model to study regulators of angiogenesis. Cell survival is improved compared to other assays by use of a modified extracellular matrix that has been validated in both short-term (2-3 days) and long-term (up to ten days) experiments. Cayman's *In Vitro* Angiogenesis Assay includes PMA and JNJ-10198409 as controls for stimulation and inhibition of angiogenesis, respectively, as well as the fluorescent dye Calcein AM for visualization of cell organization.

1 ea

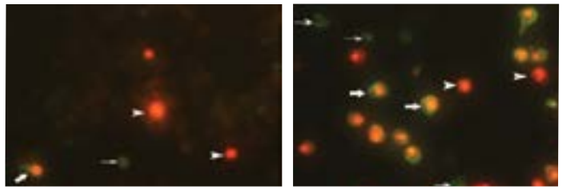


Inhibition of network formation by JNJ-10198409. *Panel A:* CAPE cells suspended in culture medium containing 0.064 µM PMA or *Panel B:* 0.064 µM PMA + 0.3 µM JNJ-10198409 were seeded at a density of 6 x 10^5 cells/well in a 96-well plate and grown in 37°C incubator for four days. On the fifth day, cells were stained with Calcein AM and the organization was examined under an inverted fluorescence microscope.

Annexin V FITC Assay Kit 600300

Stability: ≥1 year at 4°C
Summary: One of the hallmarks of the early stages of apoptosis is the redistribution of membrane phospholipids such as phosphatidylserine and phosphatidylethanolamine from the inner to outer leaflet of the membrane bilayer where they are exposed on the cell surface. Externalization of phosphatidylserine residues to the outer plasma membrane leaflet allows their detection *via* their high affinity for annexin V, a phospholipid binding protein. Cayman's Annexin-V Assay Kit employs a FITC-conjugated Annexin V as a probe for phosphatidylserine on the outer membrane of apoptotic cells. Apoptotic cells bound with fluorochrome-labeled annexin V can be visualized using fluorescence microscopy, flow cytometry, or a plate reader capable of fluorescence measurements. The reagents provided in the kit are sufficient to run 100 samples when using flow cytometry, or 500 samples when using a 96-well plate format.

100 tests



Staurosporine induces apoptosis in RAW 264.7 cells, as measured by an increase of annexin V FITC positive cells. RAW 264.7 cells treated with vehicle (control) or 8 µg/ml of staurosporine (treatment) for five hours processed for staining of dead cells and annexin V FITC. *Left Panel:* in control cells, there are a few propidium iodide positive dead cells (arrow heads) and few of these cells are from apoptosis (thick arrow, both propidium iodide and annexin V FITC positive). A thin arrow indicates a cell at an early apoptotic stage, which is annexin V FITC positive but propidium iodide negative. *Right Panel:* cells treated with 8 µg/ml of staurosporine show an increase in both propidium iodide positive cells (arrowheads), annexin V FITC positive cells (thin arrows), and cells which are both propidium iodide and annexin V FITC positive (thick arrows).

ANP32A Polyclonal Antibody 13783

Acidic Leucine-Rich Nuclear Phosphoprotein 32 Family Member A, Inhibitor-1 of Protein Phosphatase 2A, Leucine-Rich Acidic Nuclear Protein, Mapmodulin, PP32, Putative HLA-DR-Associated Protein I
Supplied as: Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: synthetic peptides corresponding to human ANP32A amino acids 87-103 and 231-246 • Host: rabbit • Cross Reactivity: (+) chimpanzee, ovine, human, and rhesus monkey ANP32A • Application(s): WB • ANP32A has been implicated in proliferation, differentiation, apoptosis, supression of transformation, inhibition of PP2A, regulation of mRNA trafficking and stability, and inhibition of acetyltransferases.

1 ea

Apaf-1 Polyclonal Antibody 160780

Apoptosis Protease-Activating Factor 1
Supplied as: 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 murine 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.

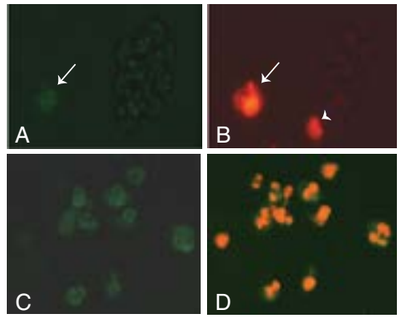
500 µl

• Also Available: **Apaf-1 Blocking Peptide** (360780) 200 µg

Apoptotic Blebs Assay Kit 10010750

Stability: ≥6 months at 4°C
Summary: Cayman's Apoptotic Blebs Assay employs a recombinant protein derived from single chain variable fragments (scFv) of an antibody which preferentially binds to the autoantigen in membrane blebs of apoptotic cells. This recombinant protein is fused to protein A allowing visualization using fluorescein-conjugated rabbit IgG. This assay is specific for cells in the execution stage of apoptosis.

1 ea



Staurosporine induces apoptosis in Jurkat cells, as measured by an increase of apoptotic blebs. *Panels A and B:* apoptotic blebs in green (A) and dead cells in red (B) taken from the same field of control cells. *Panels C and D:* show apoptotic blebs in green (C) and dead cells from apoptosis in orange (D) taken from the same field of staurosporine-treated cells.

ARC Polyclonal Antibody 160737

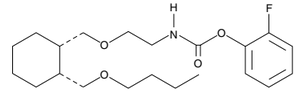
Apoptosis Repressor with CARD
Supplied as: Affinity-purified IgG **Stability:** ≥1 year at 4°C
Summary: Antigen: human ARC amino acids 191-208 • Host: rabbit • Cross Reactivity: (+) human and murine ARC • Application(s): IP and WB • ARC interacts with caspase-2 and -8 and inhibits enzymatic activity of caspase-8. ARC suppresses apoptosis induced by cell death adapters FADD and TRADD and by cell death receptors Fas, TNFR-1, and DR3.

500 µl

(+)-AS 115 10009650

MF: $C_{21}H_{32}FNO_4$ **FW:** 381.5 **Purity:** ≥98%
A solution in methyl acetate **Stability:** ≥1 year at -20°C
Summary: A single enantiomer of a potent and selective inactivator of KIAA1363, a MAGE hydrolase that is upregulated in aggressive cancers from various tissues (IC_{50} = 150 nM when tested as a racemic mixture in SK0V-3 cells); activity of the individual enantiomers of AS 115, *i.e,*. (+)-AS 115 and (-)-AS 115, has not been determined

100 µg
500 µg
1 mg
5 mg

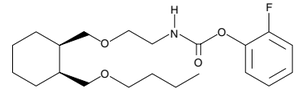


N-[2-[[(1S,2R)-2-(butoxymethyl)cyclohexyl]methoxy]ethyl]-2-fluorophenyl ester-carbamic acid

(-)-AS 115 13250

[926657-43-4]
MF: $C_{21}H_{32}FNO_4$ **FW:** 381.5 **Purity:** ≥98%
A solution in methyl acetate **Stability:** ≥1 year at -20°C
Summary: A single enantiomer of a potent and selective inactivator of KIAA1363, a MAGE hydrolase that is upregulated in aggressive cancers from various tissues (IC_{50} = 150 nM when tested as a racemic mixture in SK0V-3 cells); activity of the individual enantiomers of AS 115, *i.e.* (+)-AS 115 and (-)-AS 115, has not been determined

100 µg
500 µg
1 mg
5 mg

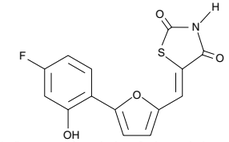


2-fluorophenyl-(2-(((1R,2S)-2-(butoxymethyl)cyclohexyl)methoxy)ethyl)carbamate

AS-252424 10009052

[900515-16-4]
MF: $C_{14}H_8FNO_4S$ **FW:** 305.3 **Purity:** ≥95%
A solution in ethanol **Stability:** ≥1 year at -20°C
Summary: A potent inhibitor of PI3K with selectivity for the γ isoform; inhibits human recombinant PI3Kγ, α, β, and δ with IC_{50} values of 30, 940, 20,000, and 20,000 nM, respectively

1 mg
5 mg
10 mg
25 mg

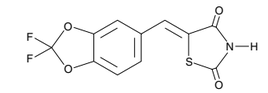


5-[5-(4-fluoro-2-hydroxy-phenyl)-furan-2-ylmethylene]-thiazolidine-2,4-dione

AS-604850 10010175

[648449-76-7]
MF: $C_{11}H_5F_2NO_4S$ **FW:** 285.2 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A selective, ATP-competitive inhibitor of PI3Kγ with IC_{50} values of 0.25, >20, >20, and 4.5 µM for the human recombinant γ, δ, β, and α isoforms, respectively

1 mg
5 mg
10 mg
25 mg

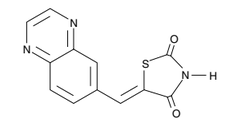


5-[(2,2-difluoro-1,3-benzodioxol-5-yl)methylene]-2,4-thiazolidinedione

AS-605240 10007707

[648450-29-7]
MF: $C_{12}H_7N_3O_2S$ **FW:** 257.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An orally active inhibitor of PI3Kγ that suppresses joint inflammation in murine models of rheumatoid arthritis; inhibits human recombinant PI3Kγ, α, β, and δ in an ATP-competitive manner with IC_{50} values of 8, 60, 270, and 300 nM, respectively

1 mg
5 mg
10 mg
50 mg

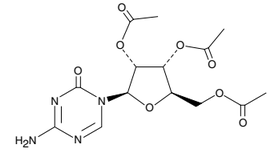


5-(6-quinoxalinylmethylene)-2,4-thiazolidinedione

2',3',5'-triacetyl-5-Azacytidine 13373

[10302-78-0]
MF: $C_{14}H_{18}N_4O_8$ **FW:** 370.3 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A prodrug form of 5-azacytidine; an inhibitor of DNA methltransferases that may reverse epigenetic methylation patterns; may be rapidly absorbed orally without formation of major metabolites in the gastrointestinal tract

5 mg
10 mg
50 mg
100 mg



4-amino-1-(2,3,5-tri-O-acetyl-β-D-ribofuranosyl)-1,3,5-triazin-2(1H)-one

Caspase Antibodies

Item No.	Item Name	Formulation	Host	Cross Reactivity	Application(s)
13907	Caspase-1 Monoclonal Antibody (Clone 14F468)	Protein G-purified IgG	Mouse, Clone 14F468	(+) Human and murine Caspase-1	IHC (paraffin-embedded sections) and WB
13906	Caspase-1 Polyclonal Antibody	Protein G-purified IgG	Rabbit	(+) Human Caspase-1	IHC (paraffin-embedded sections) and WB
13908	Caspase-2 Monoclonal Antibody (Clone 18E809.3)	Antibody in 200 µl PBS	Mouse, Clone 18E809.3	(+) Human Caspase-2	WB
13911	Caspase-3 Monoclonal Antibody (Clone 31A893)	Protein G-purified IgG	Mouse, Clone 31A893	(+) Human Caspase-3	WB
13909	Caspase-3 Monoclonal Antibody (Clone 31A1067)	Protein G-purified IgG	Mouse, Clone 31A1067	(+) Human, murine, and rat Caspase-3	IHC (frozen and paraffin-embedded sections) and WB
160745	Caspase-3 (human) Polyclonal Antibody	Peptide affinity-purified IgG	Rabbit	(+) Human, murine, baboon, and hamster Caspase-3	IHC and WB
13912	Caspase-7 Monoclonal Antibody (Clone 25B881.1)	Protein G-purified IgG	Mouse, Clone 25B881.1	(+) Human, murine, and rat Caspase-7	IHC (paraffin-embedded sections) and WB
13913	Caspase-8 Monoclonal Antibody (Clone 90A992)	Protein G-purified IgG	Mouse, Clone 90A992	(+) Human, Rhesus monkey, and chimpanzee Caspase-8	FC, IHC (paraffin-embedded sections), and WB
13914	Caspase-8 Monoclonal Antibody - biotin (Clone 90A992)	Protein G-purified IgG	Mouse, Clone 90A922	(+) Human, Rhesus monkey, and chimpanzee Caspase-8	ELISA
160790	Caspase-9 Polyclonal Antibody	Peptide affinity-purified IgG	Rabbit	(+) Human Caspase-9	WB
13915	Caspase-9 (carboxy-terminal divergent) Polyclonal Antibody	IgG	Rabbit	(+) Human, murine, and rat Caspase-9	WB
13916	Caspase-14 Monoclonal Antibody (Clone 70A1426)	Protein G-purified IgG	Mouse, Clone 70A1426	(+) Human and murine Caspase-14	FC and WB

Baicalein 70610

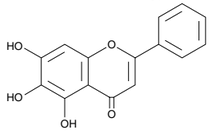
[491-67-8]

MF: $C_{15}H_{10}O_5$ **FW:** 270.2 **Purity:** ≥95%

A yellow crystalline solid **Stability:** ≥1 year at -20°C

Summary: A naturally occuring flavonoid with multiple biological activities; inhibits platelet 12-LO (IC_{50} = 0.12 µM); inhibits lipid peroxidation (IC_{50} = 5 µM); inhibits cell growth of three human hepatocellular carinoma cell lines (IC_{50} = 17-70 µg/ml)

50 mg
100 mg
500 mg
1 g



5,6,7-trihydroxyflavone

Bim/BOD (IN) Polyclonal Antibody 10011385

Supplied as: Affinity - purified IgG

Stability: ≥1 year at -20°C

Summary: Antigen: internal central human Bim amino acids • Host: rabbit • Cross Reactivity: (+) human, murine, 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, Bcl-xL, and Bcl-w and induces apoptosis.

25 µg
100 µg

BIO 13123

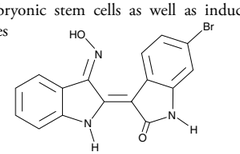
[667463-62-9] GSK 3 IX, MLS 2052

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 GSK-3α/β (IC_{50} = 5 nM); inhibition of GSK activates the Wnt-signaling pathway and sustains pluripotency in human and murine ESCs (embryonic stem cells); maintains self-renewal in human and mouse embryonic stem cells as well as induces the differentiation of neonatal cardiomyocytes

1 mg
5 mg
10 mg
25 mg



6-bromo-3-[(3E)-1,3-dihydro-3-(hydroxyimino)-2H-indol-2-ylidene]-1,3-dihydro-(3Z)-2H-indol-2-one

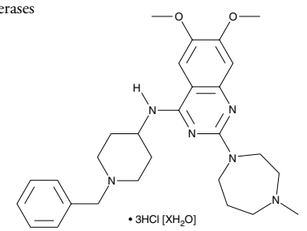
BIX01294 (hydrochloride hydrate) 13124

MF: $C_{28}H_{38}N_6O_2$ • 3HCl [XH_2O] **FW:** 600.0 **Purity:** ≥98%

A crystalline solid **Stability:** ≥2 years at -20°C

Summary: A selective inhibitor of G9a histone methyltransferase (IC_{50} = 1.7 µM); less effectively inhibits G9a-like protein (GLP; IC_{50} = 38 µM) and has no effect on other known histone methyltransferases

1 mg
5 mg
10 mg
50 mg



2-(hexahydro-4-methyl-1H-1,4-diazepin-1-yl)-6,7-dimethoxy-N-[1-(phenylmethyl)-4-piperidinyl]-4-quinazolinamine, trihydrochloride, hydrate

Capecitabine 10487

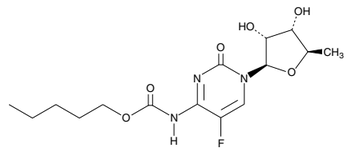
[154361-50-9] Ro 09-1978, Xeloda®

MF: $C_{15}H_{22}FN_3O_6$ **FW:** 359.4 **Purity:** ≥98%

A crystalline solid **Stability:** ≥2 years at -20°C

Summary: A fluoropyrimidine carbamate which acts as a prodrug, being enzymatically converted to 5-fluorouracil by enzymes concentrated in the liver and in cancer tissue

500 mg
1 g
5 g
10 g



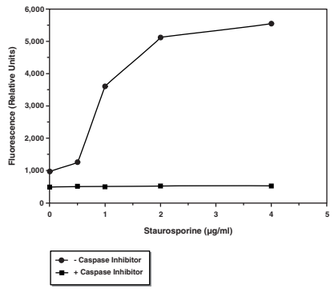
5'-deoxy-5-fluoro-N-[(pentyloxy)carbonyl]-cytidine

Caspase-3 Fluorescence Assay Kit 10009135

Stability: ≥6 months at -20°C

Summary: Caspase-3 plays a central role in the execution of apoptosis. Cayman's Caspase-3 Fluorescence Assay employs a specific caspase-3 substrate, N-Ac-DEVD-N'-MC-R110, which upon cleavage by active caspase-3, generates a highly fluorescent product that can be measured using excitation and emission wavelengths of 485 and 535 nm, respectively. Active caspase-3 is included in the kit as a positive control or as a quantitative standard.

96 wells



β-Catenin Polyclonal Antibody 100029

Supplied as: Peptide affinity-purified IgG **Stability:** ≥6 months at 4°C

Summary: Antigen: human β-catenin amino acids 43-62 • Host: rabbit • Cross Reactivity: (+) human, murine, 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.

500 µl

• Also Available: ***β*-Catenin Blocking Peptide** (300013) 200 µg

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

Supplied as: 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. The role of β-catenin in these processes is thought to be regulated by the sequential phosphorylation of Ser^{29}, Ser^{33}, Ser^{37}, and Thr^{41} by GSK3β.

1 ea

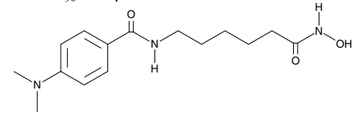
CAY10398 89740

MF: $C_{15}H_{23}N_3O_3$ **FW:** 293.4 **Purity:** ≥98%

A crystalline solid **Stability:** ≥2 years at -20°C

Summary: An inhibitor of HDAC (IC_{50} = 10 µM)

1 mg
5 mg
10 mg
25 mg



4-(dimethylamino)-N-[6-(hydroxyamino)-6-oxohexyl]-benzamide

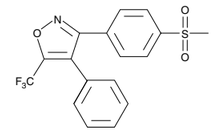
CAY10404 70210

MF: $C_{17}H_{12}F_3NO_3S$ **FW:** 367.4 **Purity:** ≥98%

A crystalline solid **Stability:** ≥2 years at -20°C

Summary: Highly selective COX-2 inhibitor (IC_{50} <1 nM); IC_{50} >500 µM (COX-1)

1 mg
5 mg
10 mg
50 mg



3-(4-methylsulphonylphenyl)-4-phenyl-5-trifluoromethylisoxazole

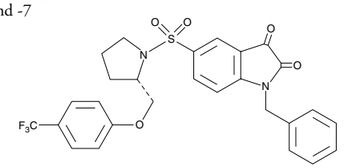
CAY10406 72510

MF: $C_{27}H_{23}F_3N_2O_5S$ **FW:** 512.5 **Purity:** ≥98%

A crystalline solid **Stability:** ≥1 year 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



(S)-1-benzyl-5-(1-[2-(phenoxy-p-trifluoromethyl)-pyrrolidynyl]-sulfonyl)-isatin

CAY10433 10005019

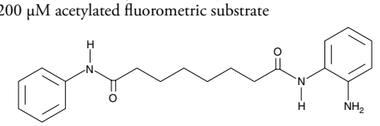
[537034-17-6] BML-210, N-phenyl-N'-(2-Aminophenyl)hexamethylenediamide

MF: $C_{20}H_{25}N_3O_2$ **FW:** 339.4 **Purity:** ≥98%

A crystalline solid **Stability:** ≥2 years at -20°C

Summary: An inhibitor of HDAC with an IC_{50} value of 30 µM when tested in HeLa cell nuclear extracts using 200 µM acetylated fluorometric substrate

1 mg
5 mg
10 mg
25 mg



N-(2-aminophenyl)-N'-phenyl-octanediamide

CAY10443 10004177

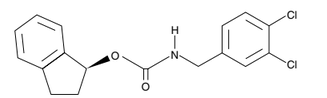
[582314-48-5] (S)-Indan-1-yl 3,4-dichlorobenzylcarbamate

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



(1S)-2,3-dihydro-1H-inden-1-yl ester [(3,4-dichlorophenyl)methyl]-carbamic acid

vol. 11 Cn

Thomas G. Brock, Ph.D.

EP_1 through EP_4: Targeting GPCRs in Cancer

The lipid mediator PGE_2, its metabolites, and its pathway enzymes COX-2 and microsomal PGE_2 synthase-1 (mPGES-1) are recognized contributors to many cancers (see related article on Page 4). Increased levels of PGE_2 and its metabolites are proven indicators of ongoing inflammation and/or cancer. COX-2 and mPGES-1 are considered viable targets for therapy. However, an alternative approach is emerging: modulating the receptors for PGE_2. PGE_2 activates four different 'E prostanoid' (EP) receptors, $EP_{1\text{-}4}$. All are G protein-coupled receptors (GPCR). Each of these receptors may have distinct roles in certain cancers that may be agonized, inactivated, or silenced therapeutically to alter the course of disease.

Over 5,000 papers have been written linking PGE_2 and cancer. Compared to this body of work, only a few papers have looked at EP receptors in cancer. Even so, there's enough data to make some key points. First, it's interesting to note that two of the four EP receptors, being G_s-coupled, overlap in their intracellular signaling, while the third, which is G_i-coupled, actually initiates signaling pathways that oppose those evoked by the other two. The fourth, a G_q-coupled receptor, uses yet another pathway. Second, in spite of their differences, all four EP receptors appear to be involved in cancer, albeit in different processes. Naturally, this might suggest a balanced four-pronged attack by PGE_2 that leads to pathogenesis. Instead, a third point that emerges from the published research is that only one of the EP receptors is responsible for mediating the majority of PGE_2's effects in many types of cancers.

EP_1, Calcium, and Cancer

EP_1 signals primarily through G_q, producing a transient rise in intracellular calcium (Figure 1). In this pathway, the interaction of PGE_2 with EP_1 converts GDP/G_q to GTP/G_q, evoking the release of GTP/G_q from the αβγ trimer and activation of phospholipase Cβ (PLCβ). PLCβ hydrolyzes phosphatidylinositol-4,5-phosphate (PIP_2) to generate diacylglycerol (DAG) and inositol-1,4,5-trisphosphate (IP_3). IP_3 binds to IP_3 receptors on the endoplasmic reticulum (ER), which act as calcium (Ca^{2+}) channels, allowing the release of Ca^{2+} from intracellular stores within the ER to the cytoplasm. DAG and Ca^{2+} activate cell-specific Ca^{2+} channels at the cell surface, producing a further increase in cytoplasmic calcium. This transient increase in intracellular Ca^{2+} alters the activity of many proteins, including several isoforms of PKC. In this way, PGE_2 evokes Ca^{2+}- and PKC-mediated effects in cells expressing EP_1. There are also reports that EP_1 can act through G_i, which is described below. The activation of EP_1 produces smooth muscle contraction, hyperalgesia, allodynia, and gastric cytoprotection. EP_1 has also been implicated in the resetting of the peripheral circadian clock, hyperthermia, sleep inhibition, and behavioral changes.

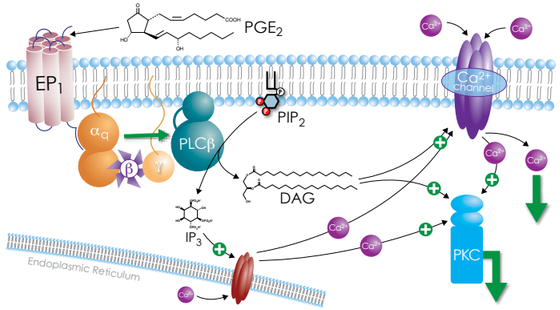


Figure 1. EP_1 signals primarily through G_q, which produces a transient rise in intracellular calcium.

Early studies with EP_1 knockout mice suggested an important role for this receptor in colon cancer: the development of aberrant crypt foci, putative preneoplastic lesions of the colon, were greatly reduced in EP_1 knockout mice treated with the colon carcinogen azoxymethane (AOM).[1] Similar results were obtained in wild type mice given an EP_1 antagonist, or in Min mice (a spontaneous colorectal cancer model) given the antagonist.[1] Longer studies demonstrated that mice lacking EP_1 displayed reduced colon cancer incidence and multiplicity as well as reduced tumor volume, compared to wild type mice, when given AOM.[2] On the other hand, an EP_1 antagonist significantly *decreased* invasive ductal adenocarcinomas in a mouse model of chemical-induced metastatic breast cancer.[3,4] EP_1 was found in breast cancers but not in normal tissues. Antagonism of EP_1 induced apoptosis of cancer cells and prevented metastasis.[3,4] PGE_2, acting through EP_1, has been shown to increase cell motility in oral cancer and chondrosarcoma cells, supporting the notion that EP_1 may increase metastasis in some cancers.[5,6] Taken together, the data suggest that selective EP_1 blockers might be useful in blocking metastasis and tumor growth in certain cancers but not others.

EP_2 through EP_4 and cAMP

The remaining three EP receptors, $EP_{2\text{-}4}$, *vie* for control of cAMP production. EP_2 and EP_4 are coupled to G_s, which directs the synthesis of cAMP, while EP_3 is G_i-linked and acts to inhibit cAMP production (Figure 2). The principle enzyme, adenylate cyclase (AC), converts ATP to cAMP. Importantly, the inhibition of cAMP production by G_i is relevant for both reducing basal cAMP production, which can be appreciable in unstimulated cells, and blocking the increased cAMP generation in cells stimulated with ligands that activate G_s-coupled receptors, like EP_2 and EP_4.

The prototypical pathway activated by cAMP involves PKA. In resting cells, PKA exists as a tetramer of two regulatory subunits holding two catalytic subunits in an inactive state. The association of cAMP with the regulatory components causes dissociation of the tetramer, allowing the free and active catalytic subunits of the kinase to phosphorylate target proteins. A second pathway that is cAMP-dependent involves the membrane associated Exchange Proteins Activated by cAMP (Epac), which include Epac-1 and Epac-2. These are two of several guanine nucleotide exchange factors (GEFs) that modify the Ras GTPase homologs Rap1 and Rap2. Like the α subunits associated with GPCRs, 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 pathway is involved in regulating a variety of different cell-specific processes, ranging from cell motility to gene expression.

As noted above, the βγ dimer, which is released from the heterotrimer following receptor activation, can also stimulate signaling pathways. There are multiple isoforms of γ, and some of those that associate with G_i can activate PLCβ. This triggers the usual signaling pathway that leads to increased intracellular Ca^{2+} and PKC activation, reminiscent of signaling through G_q. Thus, the activation of EP_3 can be monitored by measuring either cAMP or Ca^{2+}.

EP_2 and EP_3 in Cancer

The EP_2 receptor is normally involved in vascular smooth muscle relaxation, bone formation, epithelial healing, neuroprotection, and suppression of leukocyte function. This receptor has been found to be relevant to many different types of cancers. It most commonly is linked to driving angiogenesis by promoting the expression of vascular endothelial growth

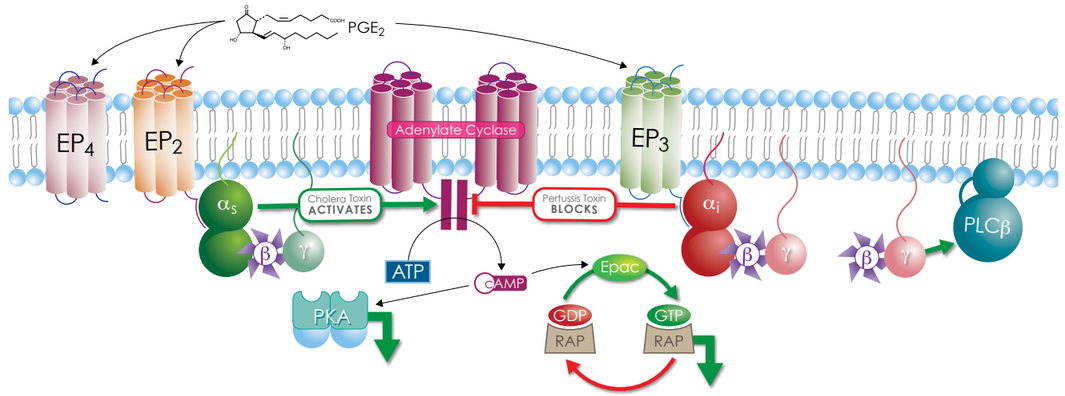


Figure 2. EP_2 and EP_4 are coupled to G_s, which directs the synthesis of cAMP, while EP_3 is G_i-linked and acts to inhibit cAMP production.

factor (VEGF).[7,8] The promoter for VEGF contains a CREB response element,[9] indicating a direct line from EP_2-mediated activation of PKA signaling to VEGF-driven angiogenesis. EP_2 signaling also up-regulates COX-2, positively amplifying PGE_2 production.[10] This receptor has also been linked to the production of myeloid-derived suppressor cells (MDSC), which are a heterogeneous population of cells that expand during cancer and suppress both the anti-tumor functions of T and NK lymphocytes as well as dendritic cell maturation.[11] MDSC also promote tumor angiogenesis.[12] These results indicate that EP_2 antagonists would be useful for reducing angiogenesis, PGE_2 production, and the development of MDSC in cancer.

The EP_3 receptor has effects on smooth muscle, neurons, and epithelium, particularly in the small intestine, kidneys, pancreas, and vascular system. It normally modulates gastric acid secretion, sodium and water reabsorption in kidneys, neurotransmitter release, and smooth muscle contraction. At least seven splice variants which vary in their cytoplasmic tails have been described; the different functions of these isoforms are unknown. Of the four EP receptors, EP_3 is the least commonly linked to cancer, with most studies examining EP_3 knockout mice or EP_3-overexpressing cells. For example, mice deficient in EP_3 show less angiogenesis in a sponge implantation model and in Lewis lung carcinomas.[13-15] The overexpression of EP_3 in human embryonic kidney cells, increases mRNA for VEGF and the VEGF receptor, VEGFR-1.[16] While these results suggest that losing EP_3 should be good for cancer, EP_3 expression is markedly decreased in human colon cancer tissues and in colon tumors induced chemically in mice and rats.[17] Similar results were found in some non-small cell lung carcinoma samples.[18] In sum, EP_3 may play an indirect role in cancer, working outside the tumor to regulate pathways that contribute to angiogenesis.

EP_4 is Important in Cancer

While it's convenient to discuss each EP receptor in turn, this gives the misleading impression that all receptors are of equivalent importance. Consider this: a PubMed search for <EP_3 cancer> turns up some 85 papers, while EP_1 or EP_2 plus cancer roughly doubles the number and <EP_4 cancer> gives over 450 publications. More focused searches in PubMed for each of the EP receptors, combined with 'lung cancer', 'colorectal cancer', or 'carcinoma', again produces many more hits for EP_4 than EP_1, EP_2, or EP_3 in each of those types of cancers. The numbers become more impressive when you realize that many papers are comparing the importance of EP_4 with other receptors in certain processes. For example, deletion of EP_4, but not EP_2, suppresses the formation of aberrant crypt foci in chemical-induced colon cancer.[19] The weight of evidence suggests that EP_4 is important in cancer.

Like EP_2, EP_4 increases cAMP, leading to phosphorylation of CREB and alteration of the expression of genes including VEGF and COX-2. Why might EP_4 be more involved in cancer than EP_2? In part, they differ in their cellular and tissue distribution, with EP_4 being more prevalent on gastric and renal epithelia. Perhaps more importantly, the expression of EP_4 can be increased in cancer tissues by diverse mechanisms.[20-22] This serves to amplify the impact of PGE_2 in cancer as well as focus the intracellular signaling down pathways activated by EP_4.

There is evidence for involvement of EP_4 in many different types of cancer. Further, EP_4 may affect essentially any cellular process, including angiogenesis, cell proliferation, apoptosis, cell motility, metastasis, and gene expression. While the majority of studies point to EP_4 as having undesirable effects in cancer, a recent study by Murn *et al.*, which portrays EP_4 as a candidate tumor suppressor, underscores the complexities of PGE_2 signaling.[23] This study shows that, in human B cells, EP_4 is a negative feedback regulator of proliferation in response to B cell receptor signals, suppressing growth in a PGE_2-dependent manner. In B cell lymphomas, EP_4 is down-regulated and growth suppression is diminished. This reminds us that EP_4 is normally expressed by diverse types of cells and evokes cell-specific actions. In fact, the effect of PGE_2-EP_4 signaling in one cell type may be the opposite of that in another cell type. These facts will need to be kept in mind as EP receptor actions are studied and therapeutic interventions are considered in the future.

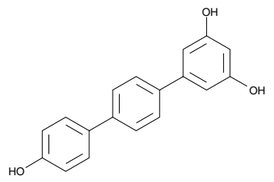
References

1. Watanabe, K., Kawamori, T., Nakatsugi, S., *et al. Cancer Res.* **59**, 5093-5096 (1999).
2. Kawamori, T., Kitamura, T., Watanabe, K., *et al. Carcinogenesis* **26(2)**, 353-357 (2005).
3. Kawamori, T., Uchiya, N., Nakatsugi, S., *et al. Carcinogenesis* **22(12)**, 2001-2004 (2001).
4. Ma, X., Kundu, N., Ioffe, O.B., *et al. Mol. Cancer Res.* **8(10)**, 1310-1318 (2010).
5. Yang, S.-F., Chen, M.-K., Hsieh, Y.-S., *et al. J. Biol. Chem.* **285(39)**, 29808-29816 (2010).
6. Liu, J.-F., Fong, Y.-C., Chang, C.-S., *et al. Mol. Cancer* **9(43)**, (2010).
7. Sung, Y.M., He, G., and Fischer, S.M. *Cancer Res.* **65(20)**, 9304-9311 (2005).
8. Kamiyama, M., Pozzi, A., Yang, L., *et al. Oncogene* **25**, 7019-7028 (2006).
9. Jeon, S.-H., Chae, B.-C., Kim, H.-A., *et al. Mol. Cells* **23(1)**, 23-29 (2007).
10. Ansari, K.M., Sung, Y.M., He, G., *et al. Carcinogenesis* **28(10)**, 2063-2068 (2007).
11. Sinha, P., Clements, V.K., Fulton, A.M., *et al. Cancer Res.* **67(9)**, 4507-4513 (2007).
12. Murdoch, C., Muthana, M., Coffelt, S.B., *et al. Nat. Rev. Cancer* **8**, 618-631 (2008).
13. Amano, H., Hayashi, I., Endo, H., *et al. J. Exp. Med.* **197(2)**, 221-232 (2003).
14. Amano, H., Ito, Y., Suzuki, T., *et al. Cancer Sci.* **100(12)**, 2318-2324 (2009).
15. Kubo, H., Hosono, K., Suzuki, T., *et al. Biomed. Pharmacother.* **64**, 101-106 (2010).
16. Taniguchi, T., Fujino, H., Israel, D.D., *et al. Biochem. Biophys. Res. Commun.* **377**, 1173-1178 (2008).
17. Shoji, Y., Takahashi, M., Kitamura, T., *et al. Gut* **53**, 1151-1158 (2004).
18. Gray, S.G., Al-Sarraf, N., Baird, A.-M., *et al. Eur. J. Cancer* **45**, 3087-3097 (2009).
19. Mutoh, M., Watanabe, K., Kitamura, T., *et al. Cancer Res.* **62**, 28-32 (2002).
20. Chell, S.D., Witherden, I.R., Dobson, R.R., *et al. Cancer Res.* **66(6)**, 3106-3113 (2006).
21. Han, S., Ritzenthaler, J.D., Wingerd, B., *et al. J. Biol. Chem.* **282(11)**, 7961-7972 (2007).
22. Oh, J.-M., Kim, S.-H., Lee, Y.-I., *et al. Carcinogenesis* **30(1)**, 141-149 (2009).
23. Murn, J., Alibert, O., Wu, N., *et al. J. Exp. Med.* **205(13)**, 3091-3103 (2008).

CAY10503 — 10008872

MF: $C_{18}H_{14}O_3$ **FW:** 278.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A proapoptotic, antiproliferative compound that is able to arrest cell cycle progression in the G_0-G_1 phase; inhibits the growth of HL60, multidrug resistant HL60R, and K562 cells with IC_{50} values of 7.0, 23, and 20 µM, respectively

1 mg
5 mg
10 mg
50 mg

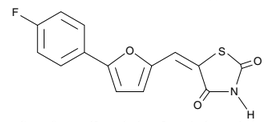


4-(4-hydroxyphenyl)phenyl-3,5-benzenediol

CAY10505 — 10009078

[328960-84-5]
MF: $C_{14}H_8FNO_3S$ **FW:** 289.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent inhibitor of PI3Kγ, selectively inhibiting the γ isoform (IC_{50} = 30 nM) better than the α, β, and δ isoforms (IC_{50} = 0.94, 20, and 20 µM, respectively); inhibits phosphorylation of PKB/Akt in murine macrophages (IC_{50} = 228 nM)

5 mg
10 mg
25 mg
50 mg

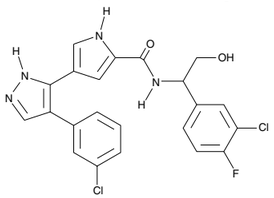


5-[[5-(4-fluorophenyl)-2-furanyl]methylene]-2,4-thiazolidinedione

CAY10561 — 10010043

[933786-58-4] Pyrazolylpyrrole ERK Inhibitor
MF: $C_{22}H_{17}Cl_2FN_4O_2$ **FW:** 459.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A selective, potent inhibitor of ERK2 (K_i = 2 nM); inhibits proliferation of Colo205 cells (IC_{50} = 0.54 µM)

500 µg
1 mg
5 mg
10 mg

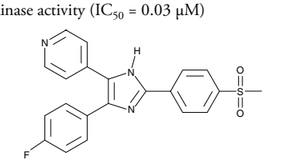


N-[1-(3-chloro-4-fluorophenyl)-2-hydroxyethyl]-4-[4-(3-chlorophenyl)-1H-pyrazol-3-yl]-1H-pyrrole-2-carboxamide

CAY10571 — 10010400

[152121-46-5]
MF: $C_{21}H_{16}FN_3O_2S$ **FW:** 393.4 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An analog of SB203580, the highly specific pyridinylimidazole inhibitor of p38 MAPK; inhibits IL-1 production in the human monocytic cell line THP (IC_{50} = 0.20 µM) and binds CSAID binding protein, a serine/threonine kinase homologous to p38, inhibiting its kinase activity (IC_{50} = 0.03 µM)

5 mg
10 mg
25 mg
100 mg

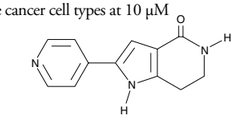


4-[5-(4-fluorophenyl)-2-[4-(methylsulfonyl)phenyl]-1H-imidazol-4-yl]-pyridine

CAY10572 — 18218

[845714-00-3] PHA 767491
MF: $C_{12}H_{11}N_3O$ **FW:** 213.2 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An inhibitor of Cdc7 kinase (IC_{50} = 10 nM) as well as CDK9 (IC_{50} = 34 nM); induces apoptotic cell death in multiple cancer cell types at 10 µM

1 mg
5 mg
10 mg
50 mg

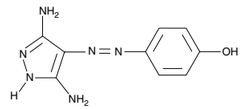


1,5,6,7-tetrahydro-2-(4-pyridinyl)-4H-pyrrolo[3,2-c]pyridin-4-one

CAY10574 — 10011247

[140651-18-9]
MF: $C_9H_{10}N_6O$ **FW:** 218.2 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent, selective inhibitor of CDK9 *in vitro* (IC_{50} = 0.35 µM); competitive inhibitor of CDK2-cyclin E with respect to ATP, with K_i and IC_{50} values of 13.3 and 20 µM, respectively

1 mg
5 mg
10 mg
50 mg

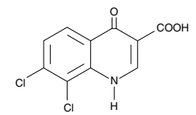


4-[(3,5-diamino-1H-pyrazol-4-yl)azo]-phenol

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

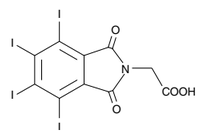


7,8-dichloro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid

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

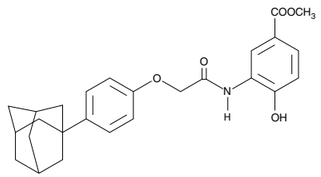


4,5,6,7-tetraiodo-1,3-dioxo-2-isoindolineacetic acid

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

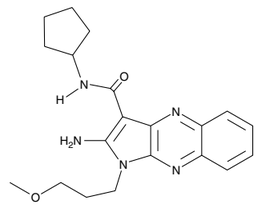


4-hydroxy-3-[[2-(4-tricyclo[3.3.1.13,7]dec-1-ylphenoxy)acetyl]amino]-benzoic acid, methyl ester

CAY10591 — 10009797

[839699-72-8] SIRT1 Activator 3, Sirtuin 1 Activator 3
MF: $C_{20}H_{25}N_5O_2$ **FW:** 367.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An activator of SIRT1 that decreases TNF-α levels from 325 pg/ml (control) to 104 and 53 pg/ml at 20 µM and 60 µM, respectively; exhibits a significant dose-dependent effect on fat mobilization in differentiated adipocytes

1 mg
5 mg
10 mg
25 mg

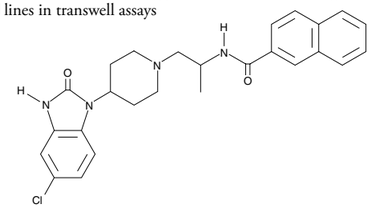


2-amino-N-cyclopentyl-1-(3-methoxypropyl)-1H-pyrrolo[2,3-b]quinoxaline-3-carboxamide

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 PLD1, both *in vitro* (IC_{50} = 46 nM) and in cells (IC_{50} = 11 nM); also effective as a PLD2 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

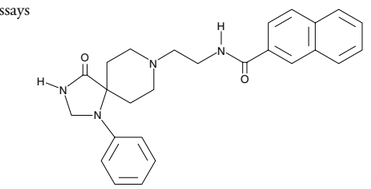


N-[2-[4-(5-chloro-2,3-dihydro-2-oxo-1H-benzimidazol-1-yl)-1-piperidinyl]-1-methylethyl]-2-naphthalenecarboxamide

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 PLD2 inhibitor, both *in vitro* (IC_{50} = 140 nM) and in cells (IC_{50} = 110 nM); also effective as a PLD1 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

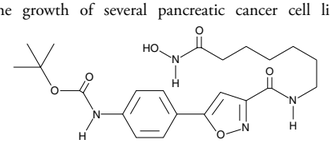


N-[2-(4-oxo-1-phenyl-1,3,8-triazaspiro[4,5]dec-8-yl)ethyl]-2-naphthalenecarboxamide

CAY10603 — 13146

[1045792-66-2]
MF: $C_{22}H_{30}N_4O_6$ **FW:** 446.5 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent and selective inhibitor of HDAC6 (IC_{50} = 0.002 nM, as compared with 271, 252, 0.42, 6851, and 90.7 nM for HDAC1, 2, 3, 8, and 10, respectively); prevents the growth of several pancreatic cancer cell lines (IC_{50} = 0.1-1 µM)

500 µg
1 mg
5 mg
10 mg

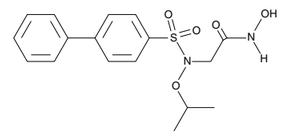


N-[4-[3-[[[7-(hydroxyamino)-7-oxoheptyl]amino]carbonyl]-5-isoxazolyl]phenyl]-1,1-dimethylethyl ester, carbamic acid

CAY10609 — 13321

[704888-90-4]
MF: $C_{17}H_{20}N_2O_5S$ **FW:** 364.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A selective inhibitor of MMP-2 demonstrating an IC_{50} value of 12 nM; significantly less potent towards MMP-1, MMP-3, MMP-7, and MMP-9 (IC_{50} = 50, 4.5, 50, and 2 µM, respectively); suppresses invasive behavior of HT1080 tumor cells grown on matrigel at 50 nM

1 mg
5 mg
10 mg
25 mg

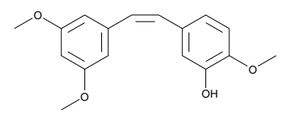


2-[([1,1'-biphenyl]-4-ylsulfonyl)(1-methylethoxy)amino]-N-hydroxy-acetamide

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 HL60R cells, a multidrug-resistant cell line derived from HL-60 cells

1 mg
5 mg
10 mg
25 mg

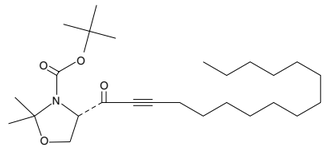


5-[(1Z)-2-(3,5-dimethoxyphenyl)ethenyl]-2-methoxy-phenol

CAY10621 13371

[120005-55-2] SPHK 1 Inhibitor [5]C
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, a sphingosine kinase over-expressed in several forms of cancer, both *in vitro* (IC_{50} = 3.3 µM) and in U937 cells over-expressing 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

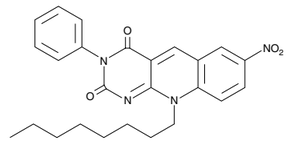


2,2-dimethyl-4S-(1-oxo-2-hexadecyn-1-yl)-1,1-dimethylethyl ester-3-oxazolidinecarboxylic acid

CAY10625 13836

[137346-42-0]
MF: $C_{25}H_{26}N_4O_4$ **FW:** 446.5 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An antagonist of the interaction between survivin and the apoptosis-promoting protein Smac/Diablo with an IC_{50} value of 2.2 µM; sensitizes cells to apoptotic stimuli

1 mg
5 mg
10 mg
50 mg

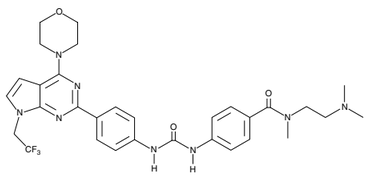


7-nitro-10-octyl-3-phenyl-pyrimido[4,5-b]quinoline-2,4(3H,10H)-dione

CAY10626 13838

[1202884-94-3]
MF: $C_{31}H_{35}F_3N_8O_3$ **FW:** 624.7 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent, dual PI3Kα/mTOR inhibitor (IC_{50}s = 0.9 and 0.6 nM, respectively); inhibits MDA361 (breast) and PC3 (prostate) tumor cell growth (IC_{50}s = <3 and 13 nM, respectively); suppresses phosphorylation of downstream targets of PI3Kα and mTOR and promotes tumor regression *in vivo*

1 mg
5 mg
10 mg
25 mg

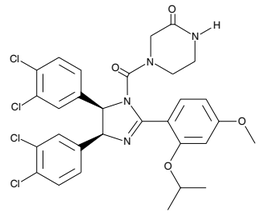


N-[2-(dimethylamino)ethyl]-N-methyl-4-[[[[4-[4-(4-morpholinyl)-7-(2,2,2-trifluoroethyl)-7H-pyrrolo[2,3-d]pyrimidin-2-yl]phenyl]amino]carbonyl]amino]-benzamide

Caylin-1 10004985

MF: $C_{30}H_{28}Cl_4N_4O_4$ **FW:** 650.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A nutlin-3 analog; inhibits the growth of HCT-116 cells at high concentrations (IC_{50} = ~7 µM); promotes the growth of HCT-116 cells ~20% at concentrations at or below 1 µM

1 mg
5 mg
10 mg
50 mg

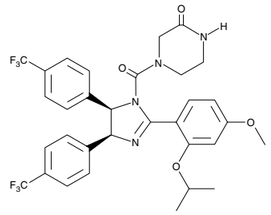


4-[4,5-bis(3,4-chlorophenyl)-2-(2-isopropoxy-4-methoxy-phenyl)-4,5-dihydro-imidazole-1-carboxyl]-piperazin-2-one

Caylin-2 10005002

MF: $C_{32}H_{30}F_6N_4O_4$ **FW:** 648.6 **Purity:** ≥98%
A crystalline solid **Stability:** ≥1 year at -20°C
Summary: A nutlin-3 analog; inhibits the growth of HCT-116 cells at high concentrations (IC_{50} = ~8 µM); promotes the growth of HCT-116 cells ~40% at concentrations at or below 1 µM

1 mg
5 mg
10 mg
50 mg

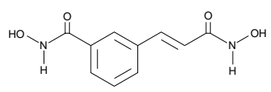


4-[4,5-bis(4-trifluoromethyl-phenyl)-2-(2-isopropoxy-4-methoxy-phenyl)-4,5-dihydro-imidazole-1-carboxyl]-piperazin-2-one

CBHA 13172

[174664-65-4] m-Carboxycinnamic Acid bis-Hydroxamide, Histone Deacetylase Inhibitor II
MF: $C_{10}H_{10}N_2O_4$ **FW:** 222.2 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: HDAC1 and HDAC3 inhibitor (ID_{50} = 0.01 and 0.07 µM, respectively, *in vitro*); induces apoptosis in nine different neuroblastoma cell lines in culture (0.5-4.0 µM) and completely suppresses neuroblastoma tumor growth in SCID mice at 200 mg/kg

5 mg
10 mg
25 mg
50 mg

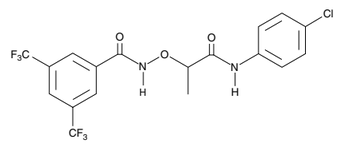


N-hydroxy-3-[3-(hydroxyamino)-3-oxo-1-propen-1-yl]-benzamide

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 serum response factor (SRF) transcription; inhibits DNA synthesis, proliferation and invasion of Rho-overexpressing cell lines at nanomolar to low micromolar concentrations

1 mg
5 mg
10 mg
25 mg

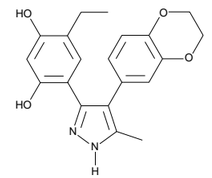


N-[2-[4(4-chlorophenyl)amino]-1-methyl-2-oxoethoxy]-3,5-bis(trifluoromethyl)-benzamide

CCT018159 10012591

[171009-07-7]
MF: $C_{20}H_{20}N_2O_4$ **FW:** 352.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A 3,4-diaryl pyrazoloresorcinol compound that inhibits the Hsp90 ATPase activity with IC_{50} values of 3.2 and 6.6 µM for human Hsp90β and yeast Hsp90, respectively; induces Hsp72 expression and decreases the expression of oncogenic client proteins such as C-RAF, ERBB2, and CDK4 in SKMEL 28 melanoma cells

1 mg
5 mg
10 mg
50 mg



4-[4-(2,3-dihydro-1,4-benzodioxin-6-yl)-5-methyl-1H-pyrazol-3-yl]-6-ethyl-1,3-benzenediol

CD4/CD8 Monoclonal FITC/PE Antibody (Clone RIV7/OKT-8) 10009852

Supplied as: CD4 mAB-FITC and CD8 mAB-PE **Stability:** ≥6 months at 4°C
Summary: Host: mouse, clones RIV7 (CD4) and OKT-8 (CD8) • Application(s): FC • This antibody pair is intended for the immunochemical detection of human $CD4^+$ and $CD8^+$ cells by FC.

1 ea

CD34 Monoclonal Antibody (Clone ICO-115) 10004835

Supplied as: Peptide affinity-purified IgG_1 **Stability:** ≥1 year at 4°C
Summary: Host: mouse, clone ICO-115 • Cross Reactivity: (+) human CD34 • Application(s): (+) FC and ICC (-) WB • CD34 is a type I transmembrane glycoprotein (M_r = 116 kDa). The antigen is expressed on stem cells and early hematopoietic progenitor cells, bone marrow stromal cells, endothelial cells, embryonic fibroblasts, and neurons. This anti-CD34 monoclonal antibody can be used for the differential staining of acute leukemia cells.

1 ea

CDK/cyclin Inhibitors

Item No.	Item Name	Target	Inhibitory Concentration
10010301	CAY10554	Cdk5 Cdk2	IC_{50} = 64 nM IC_{50} = 98 nM
10011247	CAY10574	Cdk2/cyclin E Cdk9	IC_{50} = 20 µM IC_{50} = 0.35 µM
18218	CAY10572	Cdc7	IC_{50} = 10 nM
10010302	DRB	CK2 Cdk7 Cdk8 Cdk9	IC_{50} = 4-10 µM IC_{50} = ~ 20 µM IC_{50} = ~ 20 µM IC_{50} = 3 µM
10483	Erlotinib	Cdk2	IC_{50} = 4.6 µM
13314	Indirubin-3'-monoxime	Cdk1/cyclin B Cdk2/cyclin A Cdk2/cyclin E Cdk4/cyclin D1 Cdk5/p35	IC_{50} = 180 nM IC_{50} = ~ 500 nM IC_{50} = 250 nM IC_{50} = 3.3 µM IC_{50} = 100 nM
10010239	Kenpaullone	Cdk1/cyclin B Cdk2/cyclin A Cdk5/p25	IC_{50} = 0.4 µM IC_{50} = 0.68 µM IC_{50} = 0.85 µM
10010240	Olomoucine	Cdc2/cyclin B Cdk2/cyclin A Cdk2/cyclin E Cdk/p35 kinase	IC_{50} = 7 µM IC_{50} = 7 µM IC_{50} = 7 µM IC_{50} = 3 µM
10009569	(R)-Roscovitine	Cdk2/cyclin E Cdk7/cyclin H Cdk5/p53 Cdc/cyclin B	IC_{50} = 0.1 µM IC_{50} = 0.49 µM IC_{50} = 0.16 µM IC_{50} = 0.65 µM

Cell Cycle Phase Determination Kit 10009349

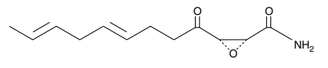
Stability: ≥6 months at -20°C
Summary: Cayman's Cell Cycle Phase Determination Kit provides an easy to use tool for studying the induction and inhibition of cell cycle progression in any cell suspension sample. The assay involves the fixation and permeabilization of the cells of interest, making possible the staining of DNA within intact cells by propidium iodide. This kit allows the investigator to determine the percentage of cells in a given sample that are within G_1/G_0, G_2, or S phase at the time of fixation, as well as to quantify cells in the sub-G_1 phase prior to apoptosis by FC.

100 tests

Cerulenin 10005647

[17397-89-6]
MF: $C_{12}H_{17}NO_3$ **FW:** 223.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An irreversible inhibitor of fatty acid synthase (FAS); causes cytoxicity and apoptosis in human cancer cell lines; causes weight loss and feeding inhibition in both high-fat diet wild type obese and leptin-deficient *ob/ob* mice

5 mg
10 mg
50 mg
100 mg

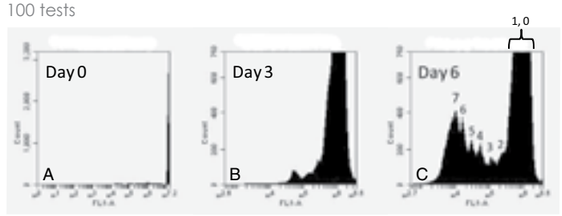


2R,3S-epoxy-4-oxo-7,10-dodecadienamide

CFSE Cell Division Assay Kit 10009853

Stability: ≥1 year at -20°C
Summary: Carboxyfluorescein diacetate, succinimidyl ester (CFDA-SE) is a novel cell-tracing fluorescent dye used to examine the proliferative activity of cells by the labeling of a parent generation and the inheritance of the label by daughter generations. CFDA-SE diffuses into cells, where the acetate groups on the molecule are cleaved to yield a highly fluorescent derivative (CFSE) that is retained in the cell and can be detected by FC. Cell division results in sequential halving of fluorescence, and up to eight divisions can be monitored before the fluorescence is decreased to the background fluorescence of unstained cells.

100 tests

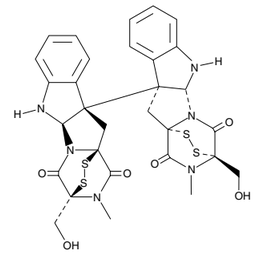


BDCM (a human DC-like cell line which can be obtained from ATCC) stimulates T cell proliferation when the cells are co-cultured together for six days. Human peripheral blood lymphocytes isolated from freshly collected blood were labeled with CFSE on Day 0. CFSE-labeled lymphocytes were then co-cultured with BDCM cells at a ratio of 25:1 in 2 ml of RPMI culture medium in a 6-well plate for three tor six days. *Panel A:* CFSE fluorescence intensity is strong at the time of staining (Day 0). *Panel B and C:* CFSE staining intensity drops rapidly in the first couple of days due to catabolism. As cell division occurs, the staining intensity stabilized (Day 3 and Day 6). *Panel C:* Eight peaks representing successive cell cycles of lymphocytes were detected after six days of BDCM stimulation (the first peak shown here actually contains two peaks representing undivided cells, peak 0, and first division cells, peak 1).

Chaetocin 13156

[28097-03-2]
MF: $C_{30}H_{28}N_6O_6S_4$ **FW:** 696.8 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A fungal mycotoxin that inhibits the Lys9-specific histone methyltransferases SU(VAR)3-9 (IC_{50} = 0.8 µM), G9a (IC_{50} = 2.5 µM), and DIM5 (IC_{50} = 3 µM); potently induces cellular oxidative stress, selectively killing cancer cells; acts as a competitive and selective substrate for thioredoxin reductase-1 (K_m = 4.6 µM)

1 mg
5 mg
10 mg

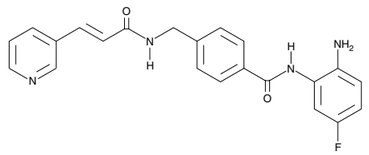


2,2',3S,3'S,5aR,5'aR,6,6'-octahydro-3,3'-bis(hydroxymethyl)-2,2'-dimethyl-[10bR,10'bR(11aS,11'aS)-bi-3,11a-epidithio-11aH-pyrazino[1',2':1,5]pyrrolo[2,3-b]indole]-1,1',4,4'-tetrone

Chidamide 13686

[743420-02-2]
MF: $C_{22}H_{19}FN_4O_2$ **FW:** 390.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An HDAC inhibitor that increases histone H3 acetylation levels in LoVo and HT29 colon cancer cells at concentrations as low as 4 µM; dose-dependently decreases the activation of several oncogenic signaling kinases and induces cell cycle arrest in colon cancer cells

1 mg
5 mg
10 mg
25 mg



N-(2-amino-5-fluorophenyl)-4-[[[1-oxo-3-(3-pyridinyl)-2-propen-1-yl]amino]methyl]-benzamide

Chromosome Associated Protein-C Polyclonal Antibody (aa 47-61) 13503

CAP-C
Supplied as: Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: synthetic peptide from human CAP-C amino acids 47-61 • Host: rabbit • Cross Reactivity: (+) human CAP-C • Application(s): WB • CAP-C plays a critical role in the structural maintenance of chromosomes, including proper condensation and segregation.

1 ea

Chromosome Associated Protein-C Polyclonal Antibody (aa 281-297) 13501

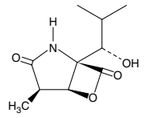
CAP-C
Supplied as: Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: synthetic peptide from human CAP-C amino acids 281-297 • Host: rabbit • Cross Reactivity: (+) human CAP-C • Application(s): WB • CAP-C plays a critical role in the structural maintenance of chromosomes, including proper condensation and segregation.

1 ea

Clasto-Lactacystin β-lactone 70988

[154226-60-5] β-Clastolactacystin, Omuralide
MF: $C_{10}H_{15}NO_4$ **FW:** 213.2 **Purity:** ≥98%
A solution in methyl acetate **Stability:** ≥2 years at -20°C
Summary: Active metabolite of lactacystin, a widely used selective inhibitor of the 20S proteasome, with at least 10 times better activity; irreversibly alkylates subunit X of the 20S proteasome

50 µg
100 µg
500 µg
1 mg

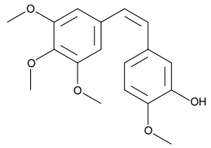


1R-[1S-1hydroxy-2-methylpropyl]-4R-methyl-6-oxa-2-azabicyclo[3.2.0]heptane-3,7-dione

Combrestatin A4 10007412

[117048-59-6] CA4, Combretastatin A4, CRC 87-09
MF: $C_{18}H_{20}O_5$ **FW:** 316.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent inhibitor of tubulin polymerization with strong inhibitory activity on tumor cell growth

5 mg
10 mg
25 mg
50 mg

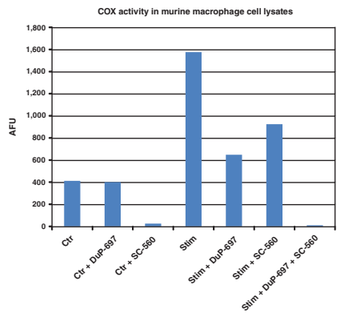


2-methoxy-5-[(1Z)-2-(3,4,5-trimethoxyphenyl)ethenyl]-phenol

COX Fluorescent Activity Assay Kit 700200

Stability: ≥1 year at -80°C
Summary: Cayman's COX Fluorescent Activity Assay provides a convenient fluorescence-based method for detecting COX-1 or COX-2 activity in both crude (cell lysates/tissue homogenates) and purified enzyme preparations. The assay utilizes the peroxidase component of COXs. In this assay, the reaction between PGG_2 and ADHP produces the highly fluorescent compound resorufin that can be analyzed using an excitation wavelength between 530-540 nm and an emission wavelength between 585-595 nm. The kit includes isozyme-specific inhibitors for distinguishing COX-2 activity from COX-1 activity.

2 x 96 wells

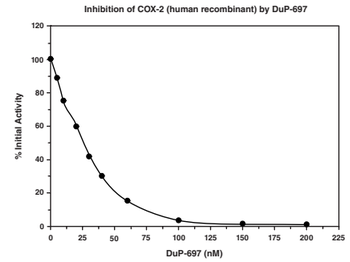


COX activity was detected in LPS/IFNγ-stimulated RAW (murine macrophage) cell lysates. COX fluorescence was compared to cells that were not treated with LPS/IFNγ (Control = Ctr). Control cells contained COX-1 and stimulated cells contained both the constitutive COX-1 and the induced COX-2 (Ctr = Control; Stim = Stimulated with LPS/IFNγ).

COX Fluorescent Inhibitor Screening Assay Kit 700100

Stability: ≥1 year at -80°C
Summary: Cayman's COX Fluorescent Inhibitor Screening Assay provides a fluorescence-based method for screening ovine COX-1 and human recombinant COX-2 for isozyme-specific inhibitors. In this assay, the peroxidase-catalyzed reaction between PGG_2 and ADHP produces the highly fluorescent compound resorufin. The kit includes both ovine COX-1 and human recombinant COX-2 in order to screen isozyme-specific inhibitors.

96 wells



• Also Available: **Colorimetric COX (ovine) Inhibitor Screening Assay Kit** (760111) 96 wells

COX Inhibitor Screening Assay Kit 560131

Stability: ≥1 year at -80°C
Summary: Cayman's COX Inhibitor Screening Assay directly measures $PGF_{2\alpha}$ produced by $SnCl_2$ reduction of COX-derived PGH_2. The prostanoid product is quantified *via* EIA using a broadly specific antibody that binds to all the major PG compounds. The kit includes both ovine COX-1 and human recombinant COX-2 in order to screen isozyme-specific inhibitors.

96 wells

• Also Available: **COX (ovine) Inhibitor Screening Assay Kit** (560101) 96 wells

COX-2 (human recombinant) 60122

PGH Synthase 2
Purity: ≥70%
Supplied as: A solution in 100 mM Tris, pH 8.0, containing 100 mM potassium chloride and 20% glycerol **Stability:** ≥6 months at -80°C
Summary: Recombinant enzyme isolated from a Baculovirus overexpression system in *Sf* 21 cells • Specific activity: >8,000 units/mg • One unit of enzyme consumes one nmol of oxygen per minute at 37°C in 0.1 M Tris-HCl buffer, pH 8.0, containing 100 µM arachidonate, 5 mM EDTA, 2 mM phenol, and 1 µM hematin

1 Kunits
2.5 Kunits
5 Kunits

COX-2 (human) Polyclonal Antibody 160107

PGH Synthase 2 Antibody
Supplied as: Peptide affinity-purified IgG **Stability:** ≥2 years at -20°C
Summary: Antigen: human COX-2 amino acids 567-599 • Host: rabbit • Cross Reactivity: (+) ovine and human COX-2; (-) COX-1 (all species) • Application(s): WB

500 µl

• Also Available: **COX-2 (human) Blocking Peptide** (360107) 200 µg
COX-2 (human) Western Ready Control (10009624) 1 ea

Goat Anti-COX-2 (human) Affinity-Purified Polyclonal Antibody 100034

PGH Synthase 2 Antibody
Supplied as: Peptide affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human COX-2 amino acids 578-596 • Host: goat • Cross Reactivity: (+) human > ovine > murine > rat COX-2; (-) COX-1 (all species) • Application(s): ICC, IHC (paraffin-embedded sections), and WB

500 µl

• Also Available: **COX-2 (human) Blocking Peptide** (360107) 200 µg

COX-2 Monoclonal Antibody (Clone CX229) 160112

PGH Synthase 2 Antibody
Supplied as: Lyophilized IgG **Stability:** ≥3 years at -20°C
Summary: Antigen: human COX-2 amino acids 580-599 • Host: mouse, clone CX229 • Isotype: IgG_1• Cross Reactivity: (+) human, ovine, and monkey COX-2; (-) murine, rat, and rabbit COX-2 and COX-1 (all species) • Application(s): ICC, IHC, and WB

1 ea

• Also Available: **COX-2 (human) Blocking Peptide** (360107) 200 µg

COX-2 Monoclonal FITC Antibody (Clone CX229) 160113

PGH Synthase 2 Antibody
Supplied as: IgG **Stability:** ≥2 years at 4°C
Summary: Antigen: human COX-2 amino acids 580-599 • Host: mouse • Isotype: IgG_1 • Cross Reactivity: (+) human and ovine COX-2; (-) murine, rat, and rabbit COX-2 and COX-1 (all species) • Application(s): FC • This product is derived by labeling the COX-2 monoclonal antibody (Item No. 160112) with fluorescein.

1 ea

COX-2 (murine) Antibodies

Item No.	Item Name
160106	COX-2 (murine) Polyclonal Antibody
160126	COX-2 (murine) Affinity-Purified Polyclonal Antibody
10010096	COX-2 (murine) Polyclonal FITC Antibody
160116	COX-2 (murine) Polyclonal Antiserum

vol. 11 Cn

Thomas G. Brock, Ph.D.

Inflammation in Cancer

Everyone has a feel for the term 'inflammation'. Who hasn't taken anti-inflammatory drugs for joint or muscle pain? Inflammatory words arouse anger. "Inflamed" connotes 'set ablaze'. But what is inflammation, physiologically? Merriam-Webster puts it this way: "a local response to cellular injury that is marked by capillary dilatation, leukocytic infiltration, redness, heat, and pain and that serves as a mechanism initiating the elimination of noxious agents and of damaged tissue". Such a definition tries to paint, in broad strokes, a term that is applied to a wide variety of processes that may be initiated by diverse triggers, may involve some or all of the listed markers, and can lead to a range of outcomes. Inflammation resulting from a bacterial infection in a skin abrasion differs distinctly from the inflammation of an arthritic joint, which in turn is vastly different from the painful, swollen response to a bee sting. In short, the devil is in the details. The same applies to the potential relevance of inflammation to cancer. Distinct types of inflammatory processes may be involved in causing, or contributing to, different types of cancer. Totally different aspects of inflammation may act during cancer, promoting such processes as metastasis or angiogenesis.

Infections, Inflammation, and Cancer

Sometimes, it may seem that infection and inflammation go hand-in-hand. However, some of the most effective pathogens are those that avoid evoking a host response. Similarly, there are many inflammatory triggers that are not infectious agents. Certainly, there are many pathogens that cause cancer and inflammatory signaling is commonly, but not always, a necessary intermediary. This topic is introduced in another article on page 48. The important point of overlap of all of these processes is host innate immunity. Bacterial infections, in particular, excite signaling pathways in tissue-resident immune cells, including dendritic cells (DC) and macrophages (Mϕ), which cause the infiltration of leukocytes from the circulation into the infected tissue. Leukocytes in neoplastic tissues were first noted in 1863 by Dr. Rudolf Virchow, who has been described as the 'Father of Modern Pathology'. He proposed that these overly abundant white cells reflected the origin of cancer at sites of chronic inflammation. While it may be argued that he was observing a correlation rather than causation, his observation certainly presaged many aspects of contemporary cancer research. Moreover, Virchow's notorious stance against a role for bacteria as a causative agent in disease, when combined with the observation of leukocytic infiltrates in tumors, nicely predicts that inflammation, in the absence of infection, must be important in the maintenance of tumors or progression of cancer. The questions become: what are these leukocytes and what are they doing?

Lymphocytes

While $CD8^+$ cytotoxic T lymphocytes (CTL) and natural killer (NK) cells play recognized roles in restraining tumor development,[1] $CD4^+$ helper cells have more diverse functions. $CD4^+$ lymphocytes differentiate into different functional subsets, depending on the cytokine signals present during activation.[2] These include the T_h1, T_h2, T_h17, and T_{reg} subsets (Figure 1). Each subset has distinct roles in cancer.

The T_h1 type of lymphocyte is induced when $CD4^+$ cells are activated in the presence of interleukin (IL)-12, IL-18, and IL-27. These cells secrete tumor necrosis factor (TNF)-α, interferon (IFN)-γ, IL-2, MCP-1, and IL-12. Through these chemical messengers, T_h1 cells regulate immune surveillance programs by increasing antigen processing and presentation by DC and Mϕ, particularly against bacteria, fungi, and viruses. In this way, T_h1 cells control the duration and magnitude of $CD8^+$ CTL activation. Moreover, T_h1 cells contribute directly to the killing of tumor cells by

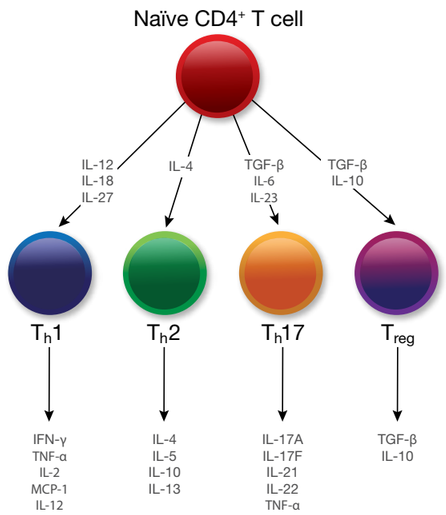


Figure 1. Naïve $CD4^+$ T cells differentiate in response to specific mediators. The resulting T cells differ in the types of mediators they produce and their roles in immunity.

secreting high levels of TNF-α and IFN-γ. Thus, T_h1 cells are decidedly anti-cancer lymphocytes.

T_h2-type $CD4^+$ cells are induced by IL-4. They secrete high levels of IL-4, IL-5, IL-10, and IL-13, which induce T cell anergy and inhibit T cell-mediated cytotoxicity. The T_h2 response is often associated with humoral responses during which high levels of pathogen-specific antibody are produced to neutralize foreign invaders, including helminths and nematodes. While T_h2 cells can inhibit apoptosis and stimulate cell proliferation in some types of cells, they are considered more relevant to allergic and antibody-mediated responses, than to cancer.

In the presence of IL-6/IL-23 and transforming growth factor (TGF)-β, $CD4^+$ cells differentiate into T_h17 lymphocytes. These secrete IL-17A, IL-17F, IL-21, TNF-α, and IL-22, mounting a defense against extracellular pathogens and regulating autoimmune disease. Naturally-occurring T_h17 cells have been found in tumors.[3] As IL-17 can promote angiogenesis and tumor growth, these cells may actually facilitate tumor survival. Interestingly, T_h17 cells can acquire T_h1-like characteristics by a variety of stimuli, including IFN-γ, IL-12, and IL-23.[4] This suggests that tumor-resident T_h17 lymphocytes may be converted into tumor-killing cells as a therapeutic approach to treating cancer.

TGF-β alone or in combination with IL-10 can generate T_{reg}, or suppressor T, cells. They secrete TGF–β and IL-10 and suppress activation of the immune system. In this way, they counter the effects of activating signals, maintaining immune system homeostasis. As they suppress the anti-tumor activities of $CD8^+$ and NK lymphocytes, increased numbers of T_{reg} cells typically correlate with poorer prognosis for survival.

While these are some of the types of T cells that develop under normal circumstances, distinctive types of lymphocytes are usually found within established tumors. These tumor-infiltrating lymphocytes (TIL) typically contain a mix of $CD4^+$, $CD8^+$, and NK cells, as well as $CD4^-/CD8^-$ cells.[5-7] $CD8^+$ TIL may secrete IL-17, like T_h17 cells, and may actually promote tumor growth.[6] The majority of TIL lack cytotoxic activity or the ability to make the immunostimulatory cytokine IFN-γ.[7] $CD4^-/CD8^-$ lymphocytes produce the anti-inflammatory cytokine IL-10, suppressing immune function within the tumor.[5] While TIL poorly fight cancer from within the tumor, they may be isolated from malignant tissue and greatly expanded *ex vivo*, then returned to the patient, where, in some cases, they effectively target and kill tumors.

Macrophages (Mϕ)

In addition to phagocytosing multitudes of bacteria, dead cells, and debris, Mϕ professionally present antigen to lymphocytes and secrete diverse mediators to modulate immune function. Resident tissue Mϕ are known by many names, including Kuppfer cells (liver), microglia (brain), osteoclasts (bone), and histiocytes (connective tissue). Like T-cells, Mϕ change phenotype and function in response to different cues (Figure 2).[8,9] The classically activated Mϕ, denoted M1 to parallel the T_h1 nomenclature for lymphocytes, are induced by inflammatory mediators, like IFN-γ and TNF-α, produced by T_h1 cells. These cells have heightened microbicidal activity. Moreover, they secrete cytokines (TNF-α, IL-12, and IL-23) that modulate T_h1 and T_h17 cell function.

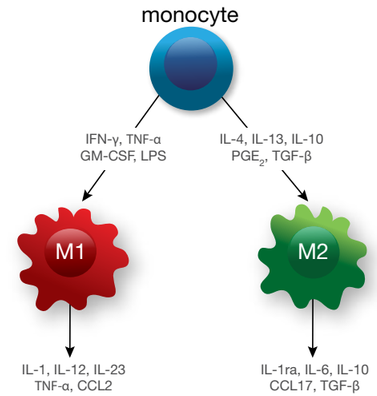


Figure 2. Monocytes from peripheral blood differentiate in response to mediators in tissues, giving rise to pro-inflammatory M1 macrophages or regulatory M2 macrophages.

Alternatively-activated, M2 Mϕ are induced by either the T_h2 cytokines IL-4 and IL-13 (M2a), immune complexes (M2b), or the immunosuppressive mediators IL-10, PGE_2, and TGF-β (M2c). M2a cells are important in mediating tissue repair, while M2c cells have regulatory or anti-inflammatory actions.

Tumor-associated Mϕ (TAMs) come from blood monocytes that are recruited at the tumor site by tumor-derived CCL2 (also known as monocyte chemotactic protein, MCP-1).[10,11] At the tumor, these monocytes become M2-like, secreting modulators that down-regulate adaptive immunity while promoting tumor growth, angiogenesis, and metastasis. These molecules include IL-10, IL-1ra, IL-1R decoy, CCL17 (TARC), CCL22, and CCL18 (PARC).

TGF-β is a pleiotropic cytokine that can be produced by tumors and have multiple pro-oncogenetic effects, including promoting angiogenesis and suppressing the immune response. It contributes to the differentiation of $CD4^+$ cells to T_h17 and T_{reg} subsets and drives Mϕ to the immunosuppressive M2c type. In addition, TGF-β inhibits the activation of naïve $CD8^+$ CTL. For these reasons, TGF-β blockers (soluble receptors or antibodies) and TGF-β receptor inhibitors have anti-tumor effects. Interestingly, TGF-β blockade also promotes an influx of tumor-associated neutrophils (TAN) with an anti-tumor phenotype.[12] Thus, therapeutic intervention at TGF-β action should facilitate tumor removal through several innate immune mechanisms.

An Epigenetic Link?

Why do tumors produce TGF-β? Epigenetics can play a pivotal role in oncogenesis. For example, overexpression of the histone methyltransferase EZH2 is associated with prostate, breast, and other cancers. EZH2 is an example of a protein which persistently alters the nucleosome, changing the ability of gene regulators to control the expression of a cluster of genes. It is the active component of polycomb repressive complex 2 (PRC2), which, at least in part, maintains a stem cell-like phenotype, as is found in the proliferative, poorly differentiated tumor cell. There is clear evidence that stem cells, and in particular the so-called 'cancer stem cell', produce TGF-β.[13] There is also some evidence that EZH2, as well as other epigenetic regulators, can increase TGF-β expression.[14,15] It remains to be determined if therapies that alter epigenetic regulators, like EZH2, effectively reduce TGF-β signaling.

Myeloid-Derived Suppressor Cells

Tumor-derived mediators, including TGF-β and PGE_2, commonly enter the blood stream and marrow, where they alter the development of myeloid stem cells and progenitors, pushing them to become active suppressor cells (Figure 3). As each type of tumor secretes a distinctive mix of messengers, differentiation of myeloid cells is highly variable and the resulting myeloid-derived suppressor cells (MDSC) are heterogeneous. However, as a group, MDSC potently suppress different aspects of immune response, including T cell function. Monocytic MDSC can associate with tumors, become TAMs, and promote angiogenesis and metastasis. Importantly, MDSC occur in many conditions in addition to cancer, such as sepsis, trauma, and infection. Because MDSC actively suppress immunity, they represent a major barrier to immunotherapies that require functional innate and adaptive immune responses.[16,17]

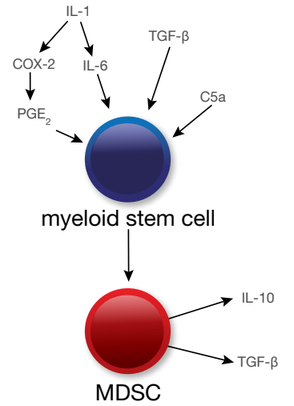


Figure 3. Tumor-derived mediators and complement component C5a alter the differentiation of myeloid stem cells to produce MDSC. MDSC secrete mediators that suppress the action of mature leukocytes and enhance tumor survival.

References

1. Dunn, G.P., Old, L.J., and Schreiber, R.D. *Immunity* **21**, 137-148 (2004).
2. Zhou, L., Chong, M.M.W., and Littman, D.R. *Immunity* **30**, 646-655 (2009).
3. Kryczek, I., Wei, S., Zou, L., *et al. J. Immunol.* **178**, 6730-6733 (2007).
4. Muranski, P. and Restifo, N.P. *Curr. Opin. Immunol.* **21(2)**, 200-208 (2009).
5. Prins, R.M., Incardona, F., Lau, R., *et al. J. Immunol.* **172**, 1602-1611 (2004).
6. Kwong, B.Y., Roberts, S.J., Silberzahn, T., *et al. J. Invest. Dermatol.* **130(6)**, 1726-1736 (2010).
7. Nguyen, L.T., Yen, P.H., Nile, J., *et al. PLoS One* **5(11)**, (2010).
8. Mantovani, A., Sica, A., and Locati, M. *Eur. J. Immunol.* **37(1)**, 14-16 (2007).
9. Mosser, D.M. and Edwards, J.P. *Nat. Rev. Immunol.* **8(12)**, 958-969 (2008).
10. Solinas, G., Germano, G., Mantovani, A., *et al. J. Leukoc. Biol.* **86(5)**, 1065-1073 (2009).
11. Siveen, K.S. and Kuttan, G. *Immunol. Lett.* **123(2)**, 97-102 (2009).
12. Fridlender, Z.G., Sun, J., Kim, S., *et al. Cancer Cell* **16(3)**, 183-194 (2009).
13. Marquardt, J.U., Factor, V.M., and Thorgeirsson, S.S. *J. Hepatol.* **53(3)**, 568-577 (2010).
14. Rao, Z.Y., Cai, M.Y., Yang, G.F., *et al. Carcinogenesis* **31(9)**, 1576-1583 (2010).
15. Shah, C.A., Wang, H., Bei, L., *et al. J. Biol. Chem.* (2010).
16. Ostrand-Rosenberg, S. *Cancer Immunol. Immunother.* **59(10)**, 1593-1600 (2010).
17. Youn, J.I. and Gabrilovich, D.I. *Eur. J. Immunol.* **40(11)**, 2969-2975 (2010).

COX-2 (ovine) 60120

PGH Synthase 2
MF: Homodimer **Purity:** ~70% **M_r:** 72 kDa (native)
Supplied in: 80 mM Tris-HCl, pH 8.0, containing 0.1% Tween 20 and 300 µM DDC **Stability:** ≥1 year at -80°C
Summary: EC: 1.14.99.1 • Isolated from sheep placenta • Specific activity: >3,000 units/mg • One unit of enzyme consumes one nmol of oxygen per minute at 37°C in 0.1 M Tris-HCl buffer, pH 8.0, containing 100 µM arachidonate, 5 mM EDTA, 2 mM phenol, and 1 µM hematin

1 Kunits
5 Kunits
10 Kunits

• Also Available: **COX-2 (ovine) Electrophoresis Standard** (360120) 1 ea

CREB (Phospho-Ser[133]) Polyclonal Antibody 10009181

cAMP-response-element-binding protein (Phospho-Ser[133])
Supplied as: Affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: phosphopeptide corresponding to amino acid residues surrounding 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 serine 133, which is required for CREB-mediated transcription.

1 ea

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

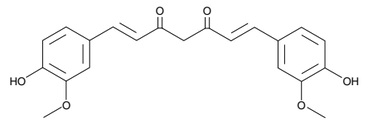
cAMP-response-element-binding protein (Phospho-Ser[133])
Stability: ≥6 months at -20°C
Summary: Cayman's CREB (Phospho-Ser[133]) Transcription Factor Assay is a non-radioactive, sensitive method for detecting CREB DNA binding activity. CREB contained in a nuclear extract or whole cell lysate binds specifically to the DNA cAMP response element immobilized to the wells of a 96-well plate. The activated CREB transcription factor complex is detected by addition of a specific primary antibody directed against Phospho-Ser[133] on CREB. A secondary antibody conjugated to HRP is used to provide a sensitive colorimetric readout at 450 nm.

96 wells

Curcumin 81025

[458-37-7] Indian Saffron, Turmeric Yellow
MF: $C_{21}H_{20}O_6$ **FW:** 368.4 **Purity:** ≥90%
A crystalline solid **Stability:** ≥2 years at room temperature
Summary: A natural product with antioxidant, antitumor, and anti-inflammatory properties

1 g
5 g
10 g
50 g



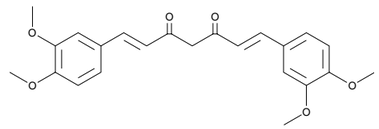
1,7-bis(4-hydroxy-3-methoxyphenyl)-1E,6E-heptadiene-3,5-dione

• Also Available: **Curcumin (technical grade)** (81025.1) 5 g, 10 g, 50 g, 100 g

dimethoxy Curcumin 10009986

[160096-59-3]
MF: $C_{23}H_{24}O_6$ **FW:** 396.4 **Purity:** ≥90%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An analog of curcumin obtained by methylation of both free phenolic groups in the parent compound; 30-fold increase in potency was observed in the growth suppression of HCT116 tumor cells following this modification

1 mg
5 mg
10 mg
50 mg

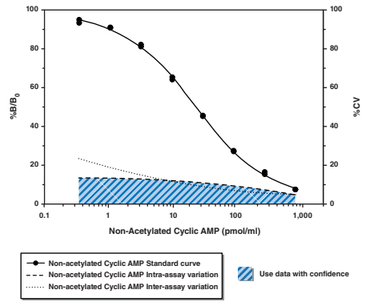


1,7-bis(3,4-dimethoxyphenyl)-1,6-heptadiene-3,5-dione

Cyclic AMP EIA Kit 581001

Adenosine 3',5'-cyclic mononucleotide
Stability: ≥1 year at -20°C
Sensitivity: 50% B/B_0: 20 pmol/ml (non-acetylated)
0.5 pmol/ml (acetylated)
80% B/B_0: 3 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.

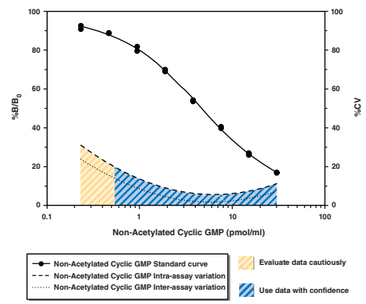
96 strip/solid wells
480 strip/solid wells



Cyclic GMP EIA Kit 581021

Guanosine 3',5'-cyclic mononucleotide
Stability: ≥1 year at -20°C
Sensitivity: 50% B/B_0: 5.2 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.

96 strip/solid wells
480 strip/solid wells



Cytokeratin Monoclonal Antibody (Clone C-11) 10004600

pan-Cytokeratin
Supplied as: Affinity-purified IgG_1 **Stability:** ≥1 year at 4°C
Summary: Host: mouse, clone C-11 • Cross Reactivity: (+) human cytokeratins 4, 5, 6, 8, 10, 13, and 18 • Application(s): FCC, ICC, IHC (paraffin-embedded sections), and WB • Cytokeratins make up a large family of proteins classified as intermediate filament polypeptides. They are subdivided into type I (acidic) and type II (basic/neutral) proteins. Under normal conditions, these proteins are found in epithelial cells as type I/type II pairs. These pairs provide cellular support as well as contribute to more dynamic processes. They undergo extensive post translational modifications, such as phosphorylation, and are important for cancer diagnostics.

1 ea

Cytokeratin Monoclonal FITC Antibody (Clone C-11) 10349

pan-Cytokeratin
Supplied as: Fluorescein-labeled IgG_1 **Stability:** ≥1 year at 4°C
Summary: Host: mouse, clone C-11 • Cross Reactivity: (+) human cytokeratins 4, 5, 6, 8, 10, 13, and 18 • Application(s): FC and IF • Cytokeratins are intermediate filament polypeptides that provide cellular support to epithelial cells as well as contribute to more dynamic processes. Cytokeratins are differentially expressed in normal and cancer cells.

1 ea

Cytokeratin Monoclonal PE Antibody (Clone C-11) 10478

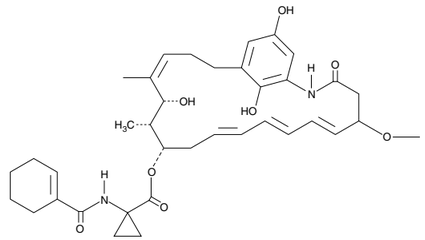
pan-Cytokeratin
Supplied as: Lyophilized purified IgG_1 **Stability:** ≥1 year at 4°C
Summary: Host: mouse, clone C-11 • Cross Reactivity: (+) human cytokeratins 4, 5, 6, 8, 10, 13, and 18 • Application(s): FC and IF • Cytokeratins are intermediate filament polypeptides that provide cellular support to epithelial cells as well as contribute to more dynamic processes. Cytokeratins are differentially expressed in normal and cancer cells.

1 ea

Cytotrienin A 63500

[189010-85-3]
MF: $C_{37}H_{48}N_2O_8$ **FW:** 648.8 **Purity:** ≥95%
A crystalline solid **Stability:** ≥1 year at -20°C
Summary: An anti-tumor agent that induces apoptosis in human promyelocytic leukemia HL-60 cells within four hours of treatment at a concentration of 100 ng/ml; activates ROS, caspase-3, p36 MBP kinase, and JNK

100 µg

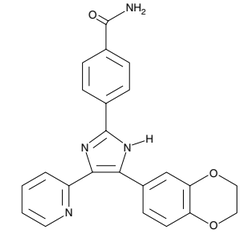


1-[(1-cyclohexen-1-ylcarbonyl)amino]-15R,22,24-trihydroxy-5R-methoxy-14R,16Z-dimethyl-3-oxo-2-azabicyclo[18.3.1]tetracosa-1(24),6E,8E,10E,16,20,22-heptaen-13S-yl ester-cyclopropanecarboxylic acid

D 4476 13305

[301836-43-1] Casein Kinase I Inhibitor
MF: $C_{23}H_{18}N_4O_3$ **FW:** 398.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A cell-permeant inhibitor of casein kinase 1 (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

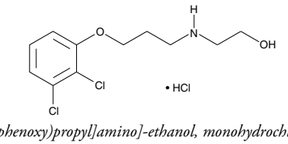


4-[4-(2,3-dihydro-1,4-benzodioxin-6-yl)-5-(2-pyridinyl)1H-imidazol-2-yl]-benzamide

2,3-DCPE (hydrochloride) 10005229

MF: $C_{11}H_{15}Cl_2NO_2$ • HCl **FW:** 300.6 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A proapoptotic compound with selectivity for cancer cells; induces apoptosis *in vitro* in various cancer cell lines (IC_{50} = 0.89-2.69 µM)

5 mg
10 mg
50 mg
100 mg



2-[[3-(2,3-dichlorophenoxy)propyl]amino]-ethanol, monohydrochloride

DcR2 Polyclonal Antibody 160755

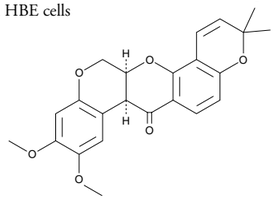
TRAIL-R4, TRUNDD
Supplied as: Affinity-purified IgG **Stability:** ≥1 year at 4°C
Summary: Antigen: human DcR2 precursor amino acids 249-263 • Host: rabbit • Cross Reactivity: (+) human DcR2 • Application(s): WB • DcR2 has an extracellular TRAIL-binding domain but lacks an intracellular death domain 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.

500 µl

(-)-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 human bronchial epithelial (HBE) cells without affecting normal HBE cells

5 mg
10 mg
25 mg
50 mg

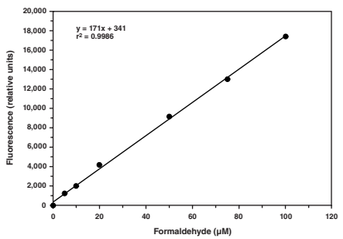


13,13aS-dihydro-9,10-dimethoxy-3,3-dimethyl-3H-[1]benzopyrano[3,4-b] pyrano[2,3-h][1]benzopyran-7(7aS)-one

Demethylase (Jumonji-type) Activity Assay Kit 700390

Stability: ≥6 months at -80°C
Summary: Lysine demethylases containing Jumonji C (JmjC) domains produce formaldehyde following 2-oxoglutarate-dependent demethylation. Cayman's Demethylase (Jumonji-type) Activity Assay provides a convenient fluorescence-based method for assaying JmjC-mediated demethylase activity from cell lysates or purified enzyme preparations. The assay is based on the production of formaldehyde during the demethylation of a peptide substrate. Cyclization of formaldehyde and acetoacetanilide in the presence of ammonia gives a fluorescent product for quantitation.

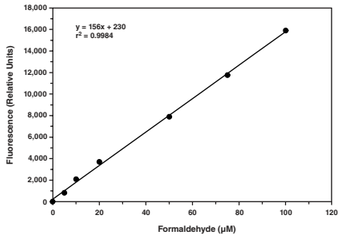
96 wells



Demethylase (LSD-type) Activity Assay Kit 700400

Stability: 6 months at -80°C
Summary: Cayman's Demethylase (LSD-type) Activity Assay provides a fluorescence-based method for assaying LSD-type demethylase activity. In this assay, formaldehyde is measured directly, eliminating the need for a coupled-enzyme reaction system. Formaldehyde, produced during demethylation of lysine 4 on a histone H3 peptide, reacts with the detection reagents provided in the kit to give a brightly fluorescent product. The assay is easy to use and can be completed in under two hours.

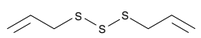
96 wells



Diallyl Trisulfide 10012577

[2050-87-5] DATS, NSC 651936
MF: $C_6H_{10}S_3$ **FW:** 178.3 **Purity:** ≥98%
A solution in acetone **Stability:** ≥1 year at -20°C
Summary: An organic polysulfide compound found in garlic that acts as an H_2S donor; reduces the survival of prostate cancer PC-3 cells (IC_{50} = 22 µM) and inhibits the growth of human colon adenocarcinoma HCT-15 cells (IC_{50} = 11.5 µM); suppresses the growth of PC-3 xenografts *in vivo* in mice and induces vascular smooth muscle relaxation

25 mg
50 mg
100 mg
250 mg

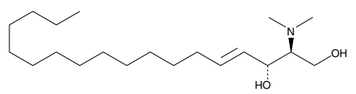


di-2-propen-1-yl trisdulfide

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 sphingosine kinase and natural metabolite of sphingosine in some cancer cell lines and tissues; inhibits sphingosine kinase from U937 cells with a K_i value of 3.1 µM

5 mg
10 mg
25 mg
50 mg

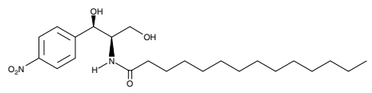


2S-(dimethylamino)-4E-octadecene-1,3R-diol

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



N-[(1R,2R)-2-hydroxy-1-(hydroxymethyl)-2-(4-nitrophenyl)ethyl]-tetradecanamide

DNA Laddering Kit 660990

Stability: ≥1 year at -20°C
Summary: Apoptosis is associated with the fragmentation of chromosomal DNA into multiples of the 180 bp nucleosomal unit, known as DNA laddering. This kit is designed to maximize extraction of small fragments of DNA with minimal contamination from intact chromatin. The isolated DNA is separated by electrophoresis and can be visualized using ethidium bromide.

24 reactions

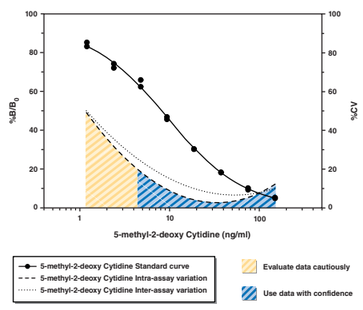
DNA Methyltransferase Antibodies

Item No.	Item Name	Formulation	Host	Cross Reactivity	Application(s)
13536	DNA Methyltransferase 1-Associated Protein 1 Polyclonal Antibody	Protein G-purified IgG	Rabbit	(+) Chimpanzee, bovine, canine, human, murine, and rat DMAP1	IHC (paraffin-embedded sections) and WB
13479	DNA Methyltransferase 1 Monoclonal Antibody (Clone 60B1220.1)	IgG	Mouse, Clone 60B1220.1	(+) Human, murine, and zebrafish DNMT1	ChIP, IHC (paraffin-embedded sections), IP, and WB
13481	DNA Methyltransferase 2 Monoclonal Antibody (Clone 102B1259.2)	Protein G-purified IgG	Mouse, Clone 102B1259.2	(+) Human and murine DNMT2	WB
13480	DNA Methyltransferase 2 Polyclonal Antibody	Protein G-purified IgG	Rabbit	(+) Human and murine DNMT2	WB
13482	DNA Methyltransferase 3a Monoclonal Antibody (Clone 64B814.1)	Protein G-purified IgG	Mouse, Clone 64B814.1	(+) Human and murine DNMT3a	ICC, IF, and WB
13483	DNA Methyltransferase 3a Monoclonal Antibody - biotinylated (Clone 64B814.1)	Protein G-purified IgG	Mouse, Clone 64B814.1	(+) Human and murine DNMT3a	ELISA
13484	DNA Methyltransferase 3a Monoclonal Antibody (Clone 64B1446)	Protein G-purified IgG	Mouse, Clone 64B1446	(+) Human and murine DNMT3a	ChIP, IF, ICC, IHC (paraffin-embedded sections), and WB
13485	DNA Methyltransferase 3b Monoclonal Antibody (Clone 52A1018)	Protein G-purified IgG	Mouse, Clone 52A1018	(+) Human and murine DNMT3b	ChIP, ICC, IF, IHC (paraffin-embedded sections), IP, and WB

DNA Methylation EIA Kit 589324

5-methyl-2-deoxy Cytidine
Stability: ≥1 year at -20°C
Sensitivity: 50% B/B_0: ~12 ng/ml • 80% B/B_0: ~3 ng/ml
Summary: DNA methylation is an important epigenetic process regulating gene expression. Methylation occurs on carbon 5 of 2-deoxy cytidine yielding the modified base 5-methyl-2-deoxy cytidine. Methylation results in long-term silencing of genes, while unmethylated regions of DNA can be actively transcribed. Cayman's DNA Methylation EIA is a competitive assay that can be used for quantification of 5-methyl-2-deoxy cytidine in urine, culture supernatants, plasma, and other sample matrices.

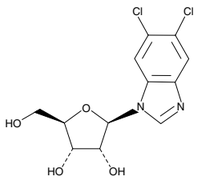
96 strip/solid wells
480 strip/solid wells



DRB 10010302

[53-85-0] Benzimidazole, NSC 401575
MF: $C_{12}H_{12}Cl_2N_2O_4$ **FW:** 319.1 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: Inhibits CKII (IC_{50} range of 4-10 µM), CDK7 (IC_{50} = ~20 µM), CDK8 (IC_{50} = ~20 µM), and CDK9 (IC_{50} = 3 µM); inhibits elongation during RNA polymerase II transcription; triggers p53-dependent apoptosis of human colon adenocarcinoma cells; inhibits trans-activated transcription of the Tat protein of HIV-1 (IC_{50} = ~4 µM)

10 mg
50 mg
100 mg
250 mg

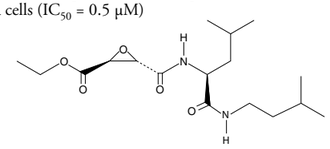


5,6-dichloro-1-β-D-ribofuranosyl-1H-benzimidazole

E-64d 13533

[88321-09-9] Aloxistatin, E-64d ethyl ester, EP 453, EST, Loxistatin, NSC 694281
MF: $C_{17}H_{30}N_2O_5$ **FW:** 342.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An irreversible, membrane-permeable inhibitor of lysosomal and cytosolic cysteine proteases; at 20-200 µM arrests human epidermoid carcinoma A431 cells at mitotic metaphase; inhibits protease-resistant protein accumulation in scrapie-infected neuroblastoma cells (IC_{50} = 0.5 µM)

1 mg
5 mg
10 mg
25 mg



3-[[[(1S)-3-methyl-1[[(3S-methylbutyl)amino]carbonyl]butyl]amino]carbonyl]-2S-oxiranecarboxylic acid, ethyl ester

EAF2 Polyclonal Antibody 10005190

ELL-Associated Factor 2, U19
Supplied as: Peptide affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human EAF2 amino acids 5-16 (AGFSHLDRRERV) • Host: rabbit • Cross Reactivity: (+) human, murine, and rat EAF2; other species not tested • Application(s): IHC (formalin-fixed paraffin-embedded sections) and WB • EAF2 is a testosterone-regulated apoptosis inducer with tumor suppressive activity. *In vivo*, overexpression of EAF2 induces massive apoptosis and inhibits prostate tumor growth.

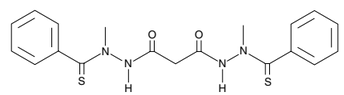
500 µl

• Also Available: **EAF Blocking Peptide** (10005732) 1 ea

Elesclomol 10011192

[488832-69-5] NSC 174939, STA 4783
MF: $C_{19}H_{20}N_4O_2S_2$ **FW:** 400.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A pro-apoptotic agent that demonstrates antitumor activity against a broad range of cancer cell types; promotes apoptosis in Hs294T melanoma cells (100 nmol/L for six hours) by rapidly generating reactive oxygen species and inducing the transcription of Hsp70 and metallothionein

1 mg
5 mg
10 mg
50 mg



1,3-bis[2-methyl-2-(phenylthioxomethyl)hydrazide]-propanedioic acid

Ellagic Acid 10569

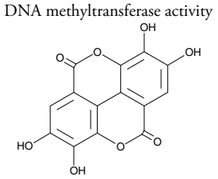
[476-66-4] Gallogen, Lagistase, TBBD

MF: $C_{14}H_6O_8$ **FW:** 302.2 **Purity:** ≥95%

A crystalline solid **Stability:** ≥2 years at -20°C

Summary: A polyphenolic antioxidant that is abundant in many fruits, vegetables, plant bark, and peels; has anti-carcinogenic, anti-mutagenic, anti-inflammatory, and organ-preserving properties; blocks methylation of H3R17 by CARM1 without significantly altering histone acetylase or DNA methyltransferase activity

100 mg
500 mg
1 g



2,3,7,8-tetrahydroxy-[1]benzopyrano[5,4,3-cde][1]benzopyran-5,10-dione

Epoxomicin 10007806

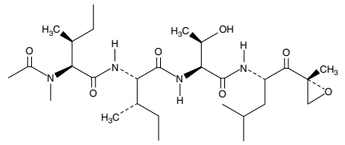
[134381-21-8] BU 4061T

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



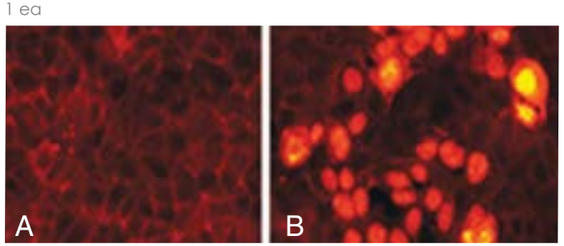
N-acetyl-N-methyl-L-isoleucyl-L-isoleucyl-N-[(1S)-3-methyl-1-[[(2R)-2-methyloxiranyl]carbonyl]butyl]-L-threoninamide

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 Kit 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 Pierce Biotechnology, Inc.) 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.

Epigenetics Enzyme Inhibitors

Item No.	Item Name	
13145	AGK2	A cell-permeable, selective inhibitor of SIRT2 (IC_{50} = 3.5 µM) that minimally affects either SIRT1 or SIRT3 at 10-fold higher levels
13144	Anacardic Acid	Inhibits the HAT activity of the transcription co-activators p300 and p300/CREB-binding protein-associated factor (pCAF) with IC_{50} values of 8.5 and 5 µM, respectively
13373	2′, 3′, 5′-triacetyl-5-Azacytidine	A prodrug form of a DNA methyltransferase inhibitor
13124	BIX01294 (hydrochloride hydrate)	A selective inhibitor of G9a HMTase (IC_{50} = 1.7 µM)
89740	CAY10398	Inhibits HDAC1 with an IC_{50} value of 10 µM
10005019	CAY10433	HDAC inhibitor with an IC_{50} value of 30 µM
13146	CAY10603	A potent, selective inhibitor of HDAC6 (IC_{50} = 0.002 nM)
13172	CBHA	A potent HDAC1 and HDAC3 inhibitor; ID_{50} values equal 0.01 and 0.07 µM *in vitro,* respectively
13156	Chaetocin	A fungal mycotoxin that inhibits the HMT SU(VAR)3-9 (IC_{50} = 0.8 µM)
13686	Chidamide	An HDAC inhibitor that increases histone H3 acetylation levels in LoVo and and HT29 colon cancer cells at concentrations as low as 4 µM
10569	Ellagic Acid	Blocks methylation of arginine 17 of histone 3 (H3R17) by CARM1
10009798	EX-527	A cell-permeable, selective inhibitor of SIRT1 (IC_{50} = 98 nM)
10576	HC Toxin	A cell-permeable, reversible inhibitor of HDACs (IC_{50} = 30 nM)
13277	(S)-HDAC-42	A potent inhibitor of HDACs (IC_{50} = 16 nM, *in vitro*)
13295	HNHA	A cell-permable inhibitor of HDAC activity (IC_{50} = 8 µM)
13174	M 344	Inhibits maize HDAC (IC_{50} = 100 nM) as well as human HDAC1 (IC_{50} = 46 nM)
13284	MS-275	Preferentially inhibits HDAC1 (IC_{50} = 300 nM) over HDAC3 (IC_{50} = 8 µM)
13176	Oxamflatin	A potent inhibitor of HDACs (IC_{50} = 15.7 nM)
13212	Pimelic Diphenylamide 106	Inhibits the class I HDACs (IC_{50} = 150, 760, 370, and 5,000 nM for HDAC1, 2, 3, and 8, respectively), but not the class II HDACs (IC_{50} > 180 µM for HDAC4, 5, and 7)
10009929	SAHA	Inhibits class I and II HDACs at around 50 nM
13178	Salermide	An inhibitor of SIRT1 and SIRT2, causing tumor-specific apoptotic cell death
10572	Scriptaid	An HDAC inhibitor that has an optimal concentration of 6-8 µM in a cell-based assay; is less toxic than trichostatin A
13121	Sodium Butyrate	HDAC inhibitor
13168	Splitomicin	An inhibitor of Sir2p HDAC activity, displaying higher activity *in vivo* (minimal IC = 0.49 µM) than *in vitro* (IC_{50} = 60 µM)
10574	Suberohydroxamic Acid	Inhibits HDAC1 (IC_{50} = 0.25 µM) and HDAC3 (IC_{50} = 0.30 µM)
13085	Tenovin-1	Inhibits the deacetylase activity of purified human SIRT1 and SIRT2

Epigenetics Enzyme Inhibitors Continued

Item No.	Item Name	
13086	Tenovin-6	Inhibits the protein deacetylase activities of purified human SIRT1, 2, and 3 *in vitro* with IC_{50} values of 21, 10, and 67 µM, respectively
89730	Trichostatin A	A potent, reversible inhibitor of HDAC1 with an IC_{50} value of 70 nM
13631	UNC0224	A potent and selective G9a HMTase inhibitor, exhibiting an IC_{50} value of 15 nM
10582	UNC0321	A highly potent, selective G9a inhibitor K_i = 63 pM
13033	Valproic Acid (sodium salt)	Inhibits class I HDACs with an IC_{50} value of ~2 mM

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

Supplied as: 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

Erlotinib 10483

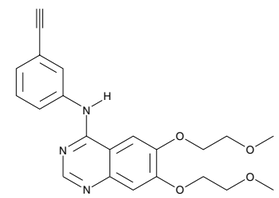
[183321-74-6] CP 358,774, NSC 718781, Tarceva™

MF: $C_{22}H_{23}N_3O_4$ **FW:** 393.2 **Purity:** ≥98%

A crystalline solid **Stability:** ≥2 years at -20°C

Summary: A tyrosine kinase inhibitor which acts on EGFR, inhibiting EGFR-associated kinase activity (IC_{50} = 2.5 µM) and tumor growth in human HN5 tumor xenografts in mice with an ED_{50} value of 9 mg/kg; drug form of Erlotinib, Tarceva™, is used to treat certain forms of cancer

250 mg
500 mg
1 g
5 g



N-(3-ethylnylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine

(±)-Equol 13184

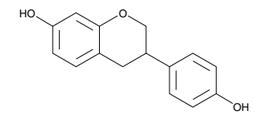
[94105-90-5]

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



3,4-dihydro-3-(4-hydroxyphenyl)-2H-1-benzopyran-7-ol

• Also Available: **(R)-Equol** (10010172) 1 mg, 5 mg, 10 mg, 25 mg

(S)-Equol (10010173) 1 mg, 5 mg, 10 mg, 25 mg

EZH1 Polyclonal Antibody 13487

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

Summary: Antigen: synthetic peptides from human EZH1 • Host: rabbit • Cross Reactivity: (+) human and murine EZH1 • Application(s): WB • EZH1 is a human homolog of the *Drosphila* gene, Enhancer of zeste, a member of the polycomb group of transcriptional repressors. It has a potential role in human development as a transcriptional regulator and a component of protein complexes that stably maintain heterochromatin.

1 ea

Farnesyl Thiosalicylic Acid 10010501

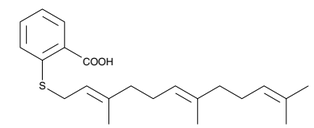
[162520-00-5] FTS, Salirasib

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



2-[[(2E,6E)-3,7,11-trimethyl-2,6,10-dodecatrien-1-yl]thio]-benzoic acid

Farnesyl Thiosalicylic Acid Amide 13175

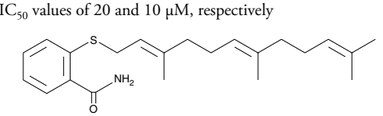
[1092521-74-8] FTS Amide, Salirasib Amide

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



2-[[(2E,6E)-3,7,11-trimethyl-2,6,10-dodecatrien-1-yl]thio]-benzamide

vol. 11 Cn

Thomas G. Brock, Ph.D.

Epigenetics in Cancer as Modeled by EZH2

Years ago, the causes of cancer boiled down to a simple dichotomy. Tumors could either be initiated by external factors, including carcinogens or viruses, or they arose from inherited internal (genetic) defects. The line between these two options became blurred with the understanding that carcinogens cause genetic changes to produce cancer. Thus, the study of cancer narrowed to a quest for the key mutations associated with each type of cancer, what aspect of the disease the gene defect produced, and what (if anything) could be done given the permanent change in DNA sequence.

Enter epigenetics. In broad terms, 'epigenetics' refers to heritable changes in gene expression that do not involve changes in DNA sequence or copy number. The more intriguing cases relate to how factors impacting parents have long-lasting effects on the health of offspring, even years after birth. A popular example centers on how the diet of the mother reprograms the genes of the fetus, without mutation, leading to persistent effects in health and development of the child.[1] In more molecular terms, epigenetic changes may involve adding or removing various "marks" on chromatin. The marks are chemical modifications, like methyl groups, and they can be added to or removed from DNA and the histones at the core of the chromatin. In theory, the pattern of marks in the genome is persistent, commonly passed down through both mitosis and meiosis. Critical events at pivotal times may alter a few key marks, producing a new epigenomic pattern of marks that are continued in ensuing cells. This system of generating lasting changes in gene expression is active in differentiation and development. Unfortunately, when it goes awry, it contributes to disease, with cancer being a prominent example.

Getting Started

In the 1990's, the Human Genome Project was sequencing human DNA and scientists were sifting through potential oncogenes. Little was written about epigenetics through the decade. Then, around the start of the new millennium, the field of epigenetics tipped, as reports of new proto-oncogenes started to appear from labs around the world. In 1999 Carlos Caldas' group from Cambridge in the UK reported the discovery of the mixed lineage leukemia homolog MLL2 associated with pancreatic and glioblastoma cell lines.[2] This gene, which is amplified in cancers, was later found to encode a lysine (K) methyltransferase (MT) (recently renamed KMT2B), which places methyl groups on lysine 4 of histone 3 in the nucleosome. From Tokyo in 2000, Inazawa and colleagues cloned GASC1 (gene amplified in squamous cell carcinoma 1) from esophageal cancer cells.[3] They identified, within the deduced amino acid sequence, potential oncogenic motifs, patterns present on other recently-described nuclear proteins involved in chromatin-mediated transcriptional regulation. We now know that GASC1 is a lysine-specific demethylase and has the function-related name of KDM4C. With the discovery of these and literally dozens of other enzymes that are active in modulating transcription by marking nucleosomes came a burst of interest in epigenetics (Figure 1).

Around the same time, Carlos Cardoso and colleagues, from Paris, and Raaphorst's team from Amsterdam characterized EZH2 (enhancer of zeste homolog 2) and linked it to cancer, although the precise function of this protein was, as yet, unknown.[4,5] EZH2 was known to be the human equivalent of the *Drosophila* protein Enhancer of Zeste (E(z)), a member of the polycomb group (PcG) proteins involved in regulating embryonic development and cell cycle control in flies. The possibility that a PcG protein was also involved in oncogenesis was a novel idea and led to an increased number of studies on EZH2 function in mammals (Figure 1). We now know that EZH2 is a histone methyltransferase, with the function-related name of KMT6.

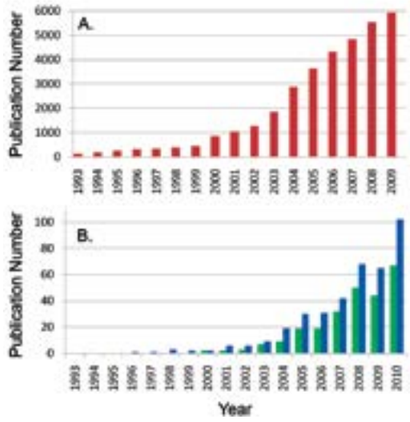


Figure 1. Annual publication rate A.) of epigenetics papers, and B.) of EZH2 papers (green: cancer-related; blue: total) in PubMed

Polycomb and Trithorax Groups

Fly geneticists have long studied homoeosis, where, during fly development, one structure is replaced by another that normally develops elsewhere. For example, a leg might form where an antenna should normally be found. In the 1970's, fly development was conceptually divided into an early 'determination' process and its observable consequences of differentiation and morphogenesis.[6] The hot question was: what occurs during 'determination'? What is the mechanism that sets in place, at an earlier time, all that is determined to unfold over an extended period of development? Part of the answer relates to genes that act on genes. The genes Polycomb (Pc) and Extra sex comb (Scx, now Antp) were first identified based on their effects on the *Drosophila* sex comb, comb-like structures on the front legs of male flies (Figure 2). The obvious increase in sex combs served as a visual indicator of underlying genetic changes and the polycomb-related proteins became known as Polycomb Group (PcG) proteins. We now know PcG proteins act in multimeric complexes to remodel chromatin and epigenetically silence gene expression. In flies, PcG proteins are best known for maintaining silent expression states of Hox genes, which specify segment identity during early embryonic development. The PcG proteins are arbitrarily distinguished from the trithorax group (trxG) proteins, as the latter can maintain active expression of Hox genes. In fact, both groups of proteins alter the access of DNA to transcriptional regulators, increasing the expression of some genes and decreasing that of others.

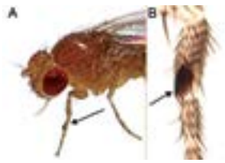


Figure 2. The sex comb on the foreleg of male fruit flies. A.) *In situ.* B.) Detail.

The specific actions of PcG and trxG proteins are diverse. Certain proteins of the complex act as adapters, binding DNA and proteins and then recruiting other complex components. By analogy, these proteins connect the active part of the complex to the site of action, much as a tool's handle (with the hand) moves the tool to where it will work (Figure 3). Functional proteins include methyltransferases, deacetylases, and RING-domain proteins which facilitate ubiquitinylation, as well as enzymes that mediate ATP-dependent remodeling of nucleosome structure, physically moving DNA to allow transcription. In addition, complexes contain structural proteins that are necessary for the enzymes to function. Like a trigger on a gun or the tip on a pipettor, they don't actually do the work, but they play important roles in getting the work done.

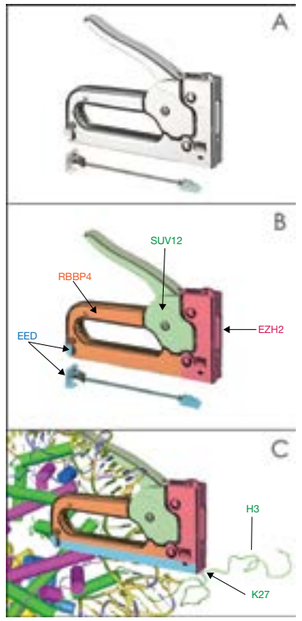


Figure 3. Important multicomponent 'complexes'. A.) A staple gun. B.) The PcG complex, PRC2. Each has adapter components for interacting with other things, a functional unit that does the work, and a part that helps, but does not drive, the function. Each 'complex' adds specific units in a directed and controlled manner. C.) The PRC2 complex interacting with the nucleosome, ready to apply a methyl group to H3K27.

Enhancing Zeste: EZH2

The different players on each of the PcG and trxG teams are not interchangeable. Instead, they interact loyally as supporting members of identifiable complexes. For example, the catalytic subunit of Polycomb Repressive Complex 2 (PRC2) is EZH2 (human) or E(z) in flies.[7,8] Suppressor of zeste-12 homolog (SUZ12) and histone-binding retinoblastoma binding protein 4 (RBBP4) form the minimal nucleosome binding module of PRC2 (Figure 3). That is, together they identify the appropriate binding site on nucleosomes and act as an adaptor by holding EZH2 in place. EED (embryonic ectoderm development) is required for the methyltransferase activity of EZH2, which targets primarily lysine 27 on histone 3 (H3K27). SUZ12, RBBP4, and EED are mammalian homologs of the Drosophila proteins Su(z)12, Extra sex combs-like (Escl), and chromatin assembly factor 1 (Caf1, also known as nucleosome-remodeling factor 55 (NURF-55)).

Several other proteins can interact around this core complex. For example, the fly Pcl (polycomblike)/ mammalian PHF1 (PHD finger 1) appears to be a facultative partner in PRC2, serving to increase KMT activity and/or facilitate binding of PRC2 to targets. The fly proteins Rpd3 (mammalian homolog: histone deacetylase 1, HDAC1) and Sir2 (mammalian homolog: sirtuin 1, SIRT1), can associate with PRC2 and remove acetyl groups from histones and other proteins. PRC2 commonly associates with a completely different team of polycomb repressive proteins, PRC1, whose active member Sex combs extra (Sce; RNF2) ubiquitinylates histone 2. Finally, PRC2 may also serve as a recruiting platform for DNA methyltransferases. Thus, the polycomb repressor complex combines protein methylation, protein deacetylation, ubiquitinylation, and DNA methylation to suppress gene expression epigenetically.

Aberrant EZH2 function has been documented in several types of human cancer, most notably prostate and breast cancer.[9,10] Most commonly, EZH2 is found to be overexpressed in cancerous tissues; overexpression may be induced by IL-6, can result from overexpression of the E2F transcription factors, or may result from gene amplification.[11-13] This presents the apparent paradox of increased activity of EZH2, which represses gene expression, somehow causing cancer. One explanation hinges on the "cancer stem cell hypothesis", which suggests that undifferentiated or dedifferentiated presursor cells may play key roles in oncogenesis.[14] EZH2-containing PRC2 is commonly found to be associated with the transcription factors Oct4, Sox2, and Nanog, which play critical roles in programming embryonic stem cell gene expression to maintain pluripotency. In this context, EZH2 is viewed as a co-repressor, inhibiting the differentiation program of stem cells and contributing to embryonic stem cell self-renewal. Complementing this suppressive effect, EZH2 activates pro-growth signaling cascades. In this way, increased expression of EZH2 pushes cell differentiation further toward a pluripotent, and oncogenic, phenotype.

Recent Developments for EZH2

A quick look at PhosphoSitePlus indicates that EZH2 can be phosphorylated on multiple sites, as documented by phosphoproteomics studies. Unfortunately, little is known about the importance of these alterations. More traditional studies report that phosphorylation of EZH2 on threonine 345 by cyclin-dependent kinases CDK1 and CDK2 (in a cell cycle-regulated fashion) increases binding of noncoding RNAs (ncRNA) to EZH2 and PRC2.[15,16] This may help PRC2 bind complementary chromatin domains, contributing to the specificity of PRC2 signaling. Curiously, CDK1 can also phosphorylate Thr 487, disrupting EZH2 binding to PRC2, inhibiting methyltransferase activity, and promoting cell differentiation.[17]

The type or amount of methylation by PRC2 may be determined by mutations on EZH2. Multiple somatic mutations of tyrosine 641 occur in B-cell lymphomas.[18] *In vitro* analysis suggests that WT EZH2 is most efficient at adding one or two methyl groups to H3K27, while the Y641 mutant efficiently di- and trimethylates the site.[19,20] The somatic mutation always occurs in one allele, producing heterozygous pairing of WT and Y641 mutants. The presence of both forms of EZH2 augments the conversion of H3K27 to the trimethylated, most repressive form. Thus mutation is a second way, after increased expression, of increasing trimethylation of H3K27, suppression of cell differentiation, and promotion of oncogenesis.

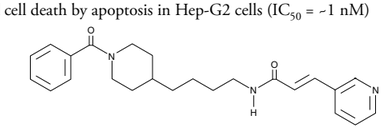
References

1. Heerwagen, M.J., Miller, M.R., Barbour, L.A., *et al. Am. J. Physiol. Regul. Integr. Comp. Physiol.* **299(3)**, R711-R722 (2010).
2. Huntsman, D.G., Chin, S.-F., Muleris, M., *et al. Oncogene* **18**, 7975-7984 (1999).
3. Yang, Z.-Q., Imoto, I., Fukuda, Y., *et al. Cancer Res.* **60**, 4735-4739 (2000).
4. Cardoso, C., Mignon, C., Hetet, G., *et al. Eur. J. Hum. Genet.* **8**, 174-180 (2000).
5. Raaphorst, F.M., van Kemenade, F.J., Blokzijl, T., *et al. Am. J. Pathol.* **157(3)**, 709-715 (2000).
6. Denell, R.E. *Genetics* **75**, 279-297 (1973).
7. Kuzmichev, A., Nishioka, K., Erdjument-Bromage, H., *et al. Genes Dev.* **16**, 2893-2905 (2002).
8. Simon, J.A. and Lange, C.A. *Mutat. Res.* **647**, 21-29 (2008).
9. Varambally, S., Dhanasekaran, S.M., Zhou, M., *et al. Nature* **419**, 624-629 (2002).
10. Kleer, C.G., Cao, Q., Varambally, S., *et al. Proc. Natl. Acad. Sci. USA* **100(20)**, 11606-11611 (2003).
11. Croonquist, P.A. and Van Ness, B. *Oncogene* **24**, 6269-6280 (2005).
12. Foster, C.S., Falconer, A., Dodson, A.R., *et al. Oncogene* **23**, 5871-5879 (2004).
13. Saramäki, O.R., Tammela, T.L., Martikainen, P.M., *et al. Genes Chromosomes Cancer* **45(7)**, 639-645 (2006).
14. Stingl, J. and Caldas, C. *Nat. Rev. Cancer* **7(10)**, 791-799 (2007).
15. Chen, S., Bohrer, L.R., Rai, A.N., *et al. Nat. Cell Biol.* **12(11)**, 1108-1114 (2010).
16. Kaneko, S., Li, G., Son, J., *et al. Genes Dev.* **24**, 2615-2620 (2010).
17. Wei, Y., Chen, Y.H., Li, L.Y., *et al. Nat. Cell Biol.* **13(1)**, 87-94 (2011).
18. Morin, R.D., Johnson, N.A., Severson, T.M., *et al. Nat. Genet.* **42(2)**, 181-185 (2010).
19. Sneeringer, C.J., Scott, M.P., Kuntz, K.W., *et al. Proc. Natl. Acad. Sci. USA* **107(49)**, 20980-20985 (2010).
20. Yap, D.B., Chu, J., Berg, T., *et al. Blood* (2010).

FK-866 13287

[658084-64-1] K 22.175
MF: $C_{24}H_{29}N_3O_2$ **FW:** 391.5 **Purity:** ≥98%
A solution in methyl acetate **Stability:** ≥2 years at -20°C
Summary: A highly specific non-competitive inhibitor of nicotinamide phosphoribosyltransferase (NAMPT) (K_i = 0.4 nM), causing gradual NAD^+ depletion; directs delayed cell death by apoptosis in Hep-G2 cells (IC_{50} = ~1 nM)

5 mg
10 mg
25 mg
50 mg

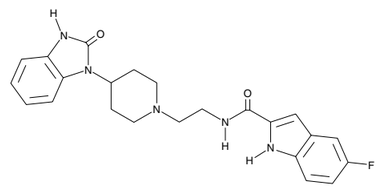


N-[4-(1-benzoyl-4-piperidinyl)butyl]-3-(3-pyridinyl)-2E-propenamide

FIPI 13563

[939055-18-2] 5-Fluoro-2-Indolyl des-Chlorohalopemide
MF: $C_{23}H_{24}FN_5O_2$ **FW:** 421.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A derivative of halopemide which potently inhibits both PLD1 (IC_{50} = 25 nM) and PLD2 (IC_{50} = 20 nM); prevents PLD regulation of F-actin cytoskeleton

1 mg
5 mg
10 mg
25 mg

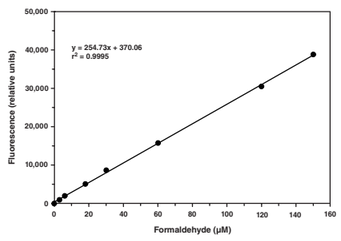


N-[2-[4-(2,3-dihydro-2-oxo-1H-benzimidazol-1-yl)-1-piperidinyl]ethyl]-5-fluoro-1H-indole-2-carboxamide

Formaldehyde Assay Kit 700380

CH_2O, Methanal
Stability: ≥6 months at Room Temperature
Summary: Cayman's Formaldehyde Assay provides a fluorescence-based method for detecting formaldehyde in urine. The cyclization between formaldehyde and acetoacetanilide (AAA) in the presence of ammonia results in a fluorescent product which is analyzed using an excitation wavelength between 365-375 nm and an emission wavelength between 465-475 nm.

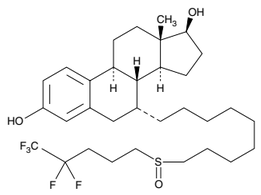
96 wells



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 estrogen receptor (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

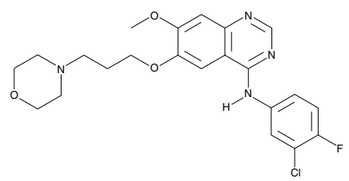


7α-[9-[(4,4,5,5,5-pentafluoropentyl)sulfinyl]nonyl]-estra-1,3,5(10)-triene-3,17β-diol

Gefitinib 13166

[184475-35-2] Iressa™, ZD1839
MF: $C_{22}H_{24}ClFN_4O_3$ **FW:** 446.9 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A selective EGFR-TK inhibitor that blocks the growth of GEO colon cancer, ZR-75-1 and MCF-10A Ha-ras breast cancer, and OVCAR-3 ovarian cancer cell lines (IC_{50}s = 0.2-0.4 µM); interferes with the intracellular kinase domain of the EGFR; used to treat advanced (or recurrent) non-small cell lung cancer

250 mg
500 mg
1 g
5 g

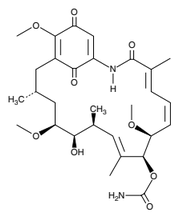


N-(3-chloro-4-fluorophenyl)-7-methoxy-6-[3-(4-morpholinyl)propoxy]-4-quinazolinamine

Geldanamycin 13355

[30562-34-6] NSC 122750
MF: $C_{29}H_{40}N_2O_9$ **FW:** 560.6 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A benzoquinone ansamycin antibiotic which binds Hsp90 and its paralog GRP94; indirectly affects diverse cellular processes, including gene expression, cell proliferation, apoptosis, and angiogenesis; inhibits c-jun expression in HT29 cells (IC_{50} = 75 nM); shows promise in cancer therapy

1 mg
5 mg
10 mg
25 mg

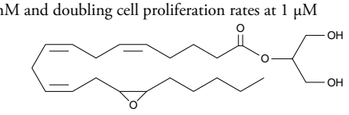


13R-hydroxy-8S,14S,19-trimethoxy-4,10,12S,16R-tetramethyl-3,20,22-trioxo-2-azabicyclo[16.3.1]docosa-1(21),4E,6E,10E,18-pentaen-9S-yl, carbamate

2-(14,15-Epoxyeicosatrienoyl) Glycerol 10009962

[848667-56-1] 2-14,15-EG
MF: $C_{23}H_{38}O_5$ **FW:** 394.5 **Purity:** ≥95%
A solution in acetonitrile **Stability:** ≥1 year at -80°C
Summary: A novel CYP450 metabolite of 2-AG in the kidney; acts as a potent mitogen for renal epithelial cells, increasing DNA synthesis in LLCPKcl4 cells at concentrations as low as 100 nM and doubling cell proliferation rates at 1 µM

25 µg
50 µg
100 µg
500 µg

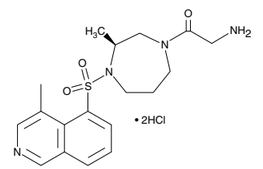


2-hydroxy-1-(hydroxymethyl)ethyl ester-13-(3-pentyloxiranyl)-5Z,8Z,11Z-tridecatrienoic acid

(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 ethanol **Stability:** ≥2 years at -20°C
Summary: A selective and potent Rho kinase inhibitor (IC_{50} = 11.8 nM for ROCK-II); poorly inhibits calcium/calmodulin kinase II, 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

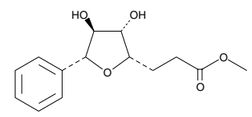


2-amino-1-[(3S)-hexahydro-3-methyl-4-[(4-methyl-5-isoquinolinyl)sulfonyl]-1H-1,4-diazepin-1-yl]-ethanone, dihydrochloride

(+)-Goniothalesdiol 10008886

[204975-45-1]
MF: $C_{14}H_{18}O_5$ **FW:** 266.7 **Purity:** ≥98%
A solution in methyl acetate **Stability:** ≥1 year at -20°C
Summary: An analog of goniothalesdiol, a tetrahydrofuran compound known to have pesticidal activity as well as significant cytotoxic effects against P388 murine leukemia cells

1 mg
5 mg
10 mg
25 mg



4,7-anhydro-2,3-dideoxy-7R-C-phenyl-D-xylo-heptonic acid, methyl ester

• Also Available: **(+)-2,5-*epi* Goniothalesdiol** (10008887) 1 mg, 5 mg, 10 mg, 25 mg

GSK3β (Phospho-Ser⁹) Polyclonal Antibody 10009374

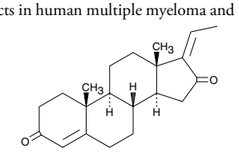
Glycogen Synthase Kinase 3β
Supplied as: Peptide affinity-purified antibody **Stability:** ≥1 year at -20°C
Summary: Antigen: phosphopeptide corresponding to amino acid residues surrounding phospho-Ser^9 of GSK3β • Host: rabbit • Cross Reactivity: (+) rat GSK3β; expected to react with human, murine, chicken, bovine, canine, non-human primate, zebrafish, and *Xenopus* GSK3β • Application(s): WB • GSK3 is a serine/threonine kinase that is involved in the regulation of many signaling pathways. GSK3β has been shown to play a key inhibitory role in both the insulin and Wnt signaling pathways. It has been suggested that Ser^9 phosphorylation underlies the inhibition of GSK3β by insulin.

1 ea

(Z)-Guggulsterone 71800

[39025-23-5]
MF: $C_{21}H_{28}O_2$ **FW:** 312.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A competitive antagonist of farnesoid X receptor (IC_{50} = 17 µM) that lowers LDL cholesterol and triglyceride levels in rodents fed a high cholesterol diet; demonstrates antitumor-promoting effects in human multiple myeloma and DU145 human prostate cancer cells

5 mg
10 mg
25 mg
50 mg

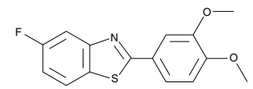


pregna-4,17Z(20)-diene-3,16-dione

GW 610 10008313

[872726-44-8] NSC 721648
MF: $C_{15}H_{12}FNO_2S$ **FW:** 289.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An antitumor benzothiazole that shows growth-inhibitory activity against several cancer cell lines

1 mg
5 mg
10 mg
50 mg

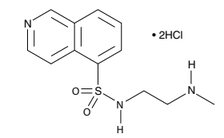


2-(3,4-dimethoxyphenyl)-5-fluoro-benzothiazole

H-8 (hydrochloride) 10010249

[113276-94-1] Protein Kinase Inhibitor H-8
MF: $C_{12}H_{15}N_3O_2S$ • 2HCl **FW:** 338.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent inhibitor of PKA and PKG that shows moderate inhibition for PKC and MLCK with K_i values of 1.2, 0.48, 15, and 68 µM, respectively; can disrupt transcriptional elongation by inhibiting cyclin C/CDK8 and cyclin H/CDK7/p36 CTD kinase activity with IC_{50} values of 47 and 6.2 µM, respectively

5 mg
10 mg
25 mg
50 mg

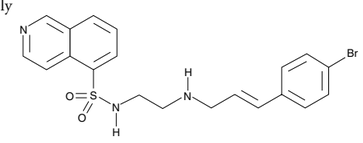


N-[2-(methylamino)ethyl]-5-isoquinolinesulfonamide, dihydrochloride

H-89 10010556

[127243-85-0] 5-Isoquinolinesulfonamide, Protein Kinase Inhibitor H-89
MF: $C_{20}H_{20}BrN_3O_2S$ **FW:** 446.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent, non-selective inhibitor of PKA with an IC_{50} value of 0.14 µM (K_i = 48 nM) that is widely used to disrupt PKA signaling; inhibits S6K1, MSK1, ROCK-II, PKBα, and MAPKAP-K1b with IC_{50} values of 0.08, 0.12, 0.27, 2.6, and 2.8 µM, respectively

5 mg
10 mg
25 mg
50 mg

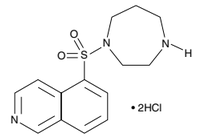


N-[2-[[3-(4-bromophenyl)-2-propen-1-yl]amino]ethyl]5-isoquinolinesulfonamide

HA-1077 (hydrochloride) 10010559

[203911-27-7] Eril, Fasudil (hydrochloride)
MF: $C_{14}H_{17}N_3O_2S$ • 2HCl **FW:** 364.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent inhibitor of ROCK-II, PRK-2, MSK1, and MAPKAP-K1b with IC_{50} values of 1.9, 4, 5, and 15 µM, respectively; has been shown to reduce blood vessel constriction, decreases pulmonary arterial pressure, inhibit tumor angiogenesis, and improve insulin signaling in a diabetic rat model; drug forms are marketed for the treatment of pulmonary arterial hypertension and stable angina

5 mg
10 mg
50 mg
100 mg

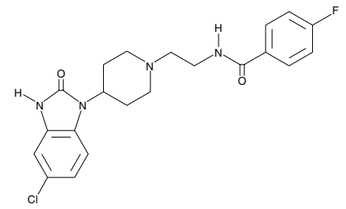


hexahydro-1-(5-isoquinolinylsulfonyl)-1H-1,4-diazepine, dihydrochloride

Halopemide 13205

[59831-65-1] NSC 354856, R34301
MF: $C_{21}H_{22}ClFN_4O_2$ **FW:** 416.2 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent inhibitor of PLD, inhibiting human PLD1 and PLD2 *in vitro* (IC_{50} = 220 and 310 nM, respectively) and PLD activity in cells; inhibits the dopamine receptor

1 mg
5 mg
10 mg
25 mg



N-[2-[4-(5-chloro-2,3-dihydro-2-oxo-1H-benzimidazol-1-yl)-1-piperidinyl]-ethyl]-4-fluoro-benzamide

HAT Inhibitor Screening Assay Kit 10006515

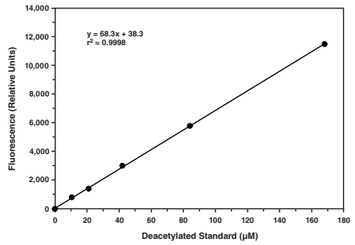
Histone Acetyltransferase
Stability: ≥6 months at -20°C
Summary: Cayman's HAT Inhibitor Screening Assay provides a fast, fluorescence-based method for evaluating pCAF HAT inhibitors. The procedure requires only three easy steps, all performed in the same microplate resulting in formation of a highly fluorescent product that is detected using excitation and emission wavelengths of 360-390 and 450-470 nm, respectively.

96 wells

HDAC Activity Assay Kit 10011563

Stability: ≥6 months at -80°C
Summary: Cayman's HDAC Activity Assay provides a fast, fluorescence-based method for measuring class I and II HDAC activity. The procedure requires only two easy steps, both performed in the same microplate. The fluorescent reaction product is easily analyzed using a plate reader with excitation wavelengths between 340-360 nm and emission wavelengths between 440-465 nm.

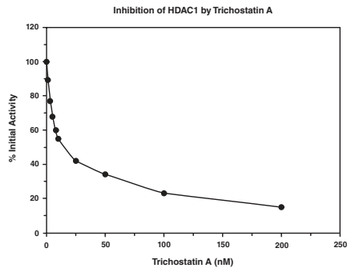
96 wells



HDAC1 Inhibitor Screening Assay Kit 10011564

Stability: ≥6 months at -80°C
Summary: Cayman's HDAC1 Inhibitor Screening Assay provides a fast, fluorescence based method for screening HDAC1 inhibitors. The procedure requires only two easy steps, both performed in the same microplate. The fluorescent reaction product is analyzed using excitation wavelengths between 340-360 nm and emission wavelengths between 440-465 nm. Sufficient purified HDAC1 is provided for 100 tests.

96 wells



HDAC Antibodies

Item No.	Item Name	Formulation	Host	Cross Reactivity	Application(s)
13491	HDAC1 Polyclonal Antibody	Protein G-purified IgG	Rabbit	(+) human HDAC1	WB
13493	HDAC3 Polyclonal Antibody	Protein G-purified IgG	Rabbit	(+) Human HDAC3	ChIP, IP, and WB
13494	HDAC4 Polyclonal Antibody	Protein G-purified IgG	Rabbit	(+) Human and murine HDAC4	ChIP, IP and WB
13499	HDAC6 Polyclonal Antibody	Protein G-purified IgG	Rabbit	(+) Human and murine HDAC6	ChIP, IP, and WB
13500	HDAC7 (Phospho-Ser^{155}) Polyclonal Antibody	Peptide-purified IgG	Rabbit	(+) Chimpanzee, bovine, canine, human, monkey, murine, and rat HDAC7	WB
13504	HDAC11 Polyclonal Antibody	Protein G-purified IgG	Rabbit	(+) Human, murine, and rat HDAC11	WB

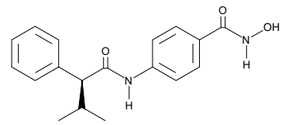
HDAC Enzymes

Item No.	Item Name	Source	M_r	Purity
10009231	HDAC1 (human recombinant)	Recombinant protein expressed using a baculovirus expression system	~ 79.9 kDa	≥10% by SDS-PAGE
10009377	HDAC2 (human recombinant)	Recombinant protein expressed using a baculovirus expression system	~ 60 kDa	≥70% by SDS-PAGE
10009232	HDAC3/NCOR2 (human recombinant)	Recombinant C-terminal His-tag expressed using a baculovirus expression system	~ 49.7 kDa	≥50%
10009652	HDAC4 (human recombinant)	N-terminal GST-tagged using a baculovirus expression system	~75.2 kDa	≥50% by SDS-PAGE
10009379	HDAC5 (human recombinant)	Recombinant C-terminal His-tag using a baculovirus expression system	~ 51 kDa	≥90% by SDS-PAGE
10009465	HDAC6 (human recombinant)	Recombinant N-terminal GST-tag using a baculovirus expression system	~ 159 kDa	≥80%
19380	HDAC8 (human recombinant)	Recombinant C-terminal His-tag expressed in *E.coli*	45.3 kDa	≥95%
10009466	HDAC9 (human recombinant)	Recombinant C-terminal His-tag using a baculovirus expression system	~ 50.7 kDa	≥95%

(S)-HDAC-42 13277

[935881-37-1] AR42
MF: $C_{18}H_{20}N_2O_3$ **FW:** 312.4 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent inhibitor of HDACs (IC_{50} = 16 nM *in vitro*); decreases the viability of prostate cancer cell lines (IC_{50} = 0.40 µM); strongly suppresses the growth of PC-3 tumor xenografts

1 mg
5 mg
10 mg
25 mg



N-[4-[(hydroxyamino)carbonyl]phenyl]-αS-(1-methylethyl)-benzeneacetamide

Hepsin Polyclonal Antibody (aa 241-260) 100022

Supplied as: Peptide affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human hepsin amino acids 241-260 • Host: rabbit • Cross Reactivity: (+) human hepsin; other species produce bands of unknown identity • Application(s): IHC and WB • Hepsin is a type II membrane-associated protein that has an extracellular proteolytic domain and exhibits low sequence homology to other known proteases. Hepsin overexpression is observed in prostate, breast, kidney, and ovarian cancers and due to low homology to other known proteases may provide a unique target for pharmacological therapy. Hepsin is necessary for cell growth *in vitro* and may play a role in metastatic expansion by factor VII activation.

500 µl

• Also Available: **Hepsin Blocking Peptide (aa 241-260)** (100024) 200 µg

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

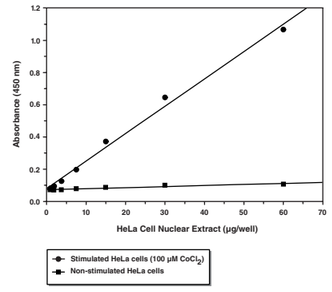
Supplied as: Peptide affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: HIF-1α C-terminal amino acids 809-826 • Host: rabbit • Cross Reactivity: (+) human, murine, and simian HIF-1α • Application(s): (+) WB; (-) ICC and IP • HIF-1α is a transcription factor that accumulates under 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.

500 µl

HIF-1α Transcription Factor Assay Kit 10006910

Stability: ≥6 months at -80°C
Summary: The HIF-1α 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.

96 wells



Histone H2B (human recombinant) 10262

Purity: ≥95%
Supplied as: A lyophilized powder **Stability:** ≥6 months at -80°C
Summary: Source: recombinant protein expressed in *E. coli* • M_r: 13.7 kDa • Histone 2H2B is one of the core nucleosomal histones, it undergoes many modifications which include acetylation, methylation, and phosphorylation that are important for regulation of gene transcription.

50 µg
100 µg
250 µg
1 mg

Histone Antibodies

Item No.	Item Name	Formulation	Host	Cross Reactivity	Application(s)
13535	Histone H2A Polyclonal Antibody	Protein G-purified IgG	Rabbit	(+) Human and murine Histone H2A	ELISA and WB
13538	Histone H2B (C-Term) Polyclonal Antibody	Protein G-purified IgG	Rabbit	(+) Chicken, canine, *Drosophila*, human, most mammals, murine, rat, and zebrafish Histone H2B	WB
13539	Histone H2B (N-Term) Polyclonal Antibody	Protein G-purified IgG	Rabbit	(+) Human Histone H2B	WB
13540	Histone H3 (Phospho-Ser^{28}) Monoclonal Antibody (Clone 117C826)	Protein G-purified IgG	Mouse, clone 117C826	(+) Human Histone H3	WB
13784	Histone H3.3 Polyclonal Antibody	Protein A-purified IgG	Rabbit	(+) Chicken, ovine, *Drosophila*, equine, human, murine, and opossum Histone H3.3	IHC and WB
13543	Histone H4 Polyclonal Antibody	Protein G-purified IgG	Rabbit	(+) Human Histone H4	WB

Histone H3 (human recombinant) 10263

Purity: ≥95%
Supplied as: A lyophilized powder **Stability:** ≥6 months at -80°C
Summary: Source: recombinant protein, expressed in *E. coli* • M_r: 15.5 kDa • Histone H3 is one of the core nucleosomal histones, it undergoes many modifications which include acetylation, methylation, and phosphorylation that are important for regulation of gene transcription.

50 µg
100 µg
250 µg
1 mg

Histone H4 (human recombinant) 10264

Purity: ≥95%
Supplied as: A lyophilized powder **Stability:** ≥6 months at -80°C
Summary: Source: recombinant protein, expressed in *E. coli* • M_r: 11.5 kDa • Histone H4 is one of the core nucleosomal histones. The N-terminal tail of histone H4 undergoes many modifications which include acetylation, methylation, and phosphorylation that are important for regulation of gene transcription.

50 µg
100 µg
250 µg
1 mg

Histone H4K20 Peptide 10380

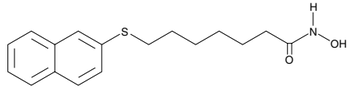
Histone 4 amino acids 15-24, SET8 Methyltransferase Acceptor Peptide
Supplied as: A lyophilized peptide **Stability:** ≥1 year at -20°C
Summary: Contains a lysine at position 20 which is a substrate or acceptor peptide for the lysine methyltransferases KMT5A (SET8) and KMT5B (SUV4-20H1)

1 mg
5 mg

HNHA 13295

[926908-04-5] Histone Deacetylase Inhibitor VI
MF: $C_{17}H_{21}NO_2S$ **FW:** 303.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A cell-permeable inhibitor of HDAC activity (IC_{50} = 100 nM)

5 mg
10 mg
25 mg
50 mg



N-hydroxy-7-(2-naphthalenylthio)-heptanamide

Hsp90α (human recombinant) 10202

Heat Shock Protein 90α, Hsp84
Purity: ≥80%
Supplied in: 50 mM sodium phosphate, pH 7.2, containing 100 mM sodium chloride, 5 mM magnesium chloride, 1 mM DTT, and 20% glycerol
Stability: ≥6 months at -80°C
Summary: Source: recombinant N-terminal His-tagged protein expressed in *E. coli* • M_r: 87 kDa • Hsp90, a molecular chaperone, forms either homo- or heterodimers of the α and β isoforms. These bind protein substrates that are unfolded and/or misfolded to assist in folding and to prevent aggregation.

50 µg
100 µg
250 µg

Hsp90β (human recombinant) 10342

Heat Shock Protein 90β, Hsc90, Hsp90 AB1
Purity: ≥85%
Supplied in: 50 mM sodium phosphate, pH 7.2, containing 100 mM sodium chloride, 5 mM magnesium chloride, 1 mM DTT, and 20% glycerol
Stability: ≥6 months at -80°C
Summary: Source: recombinant N-terminal His-tagged protein expressed in *E. coli* • M_r: 85.6 kDa • Hsp90, a molecular chaperone, forms either homo- or heterodimers of the α and β isoforms. These bind protein substrates that are unfolded and/or misfolded to assist in folding and to prevent aggregation.

25 µg
50 µg
100 µg

I2PP2A/SET Polyclonal Antibody 13782

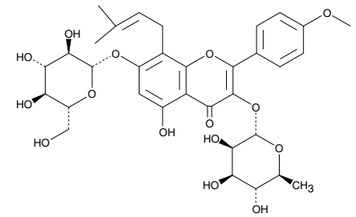
Inhibitor of Granzyme A-activated DNase, PHAPII, Phosphatase 2A Inhibitor, Template-Activating Factor I
Supplied as: Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: synthetic peptides from human I2PP2A/SET amino acids 79-94 and 148-164 • Host: rabbit • Cross Reactivity: (+) human I2PP2A/SET • Application(s): WB • I2PP2A/SET is a multitasking protein, involved in apoptosis, transcription, nucleosome assembly, and histone binding. The SET gene produces two isoforms from transcript variants. Isoform 1 and 2 interact directly with each other and with ANP32A within the tripartite inhibitor of acetyltransferases complex, inhibiting EP300/CREBBP and PCAF-mediated acetylation of histones. The two isoforms differ in their amino termini but are identical through the regions used as antigens for preparing this antibody.

1 ea

Icariin 13624

[489-32-7]
MF: $C_{33}H_{40}O_{15}$ **FW:** 676.6 **Purity:** ≥97%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An inhibitor of human recombinant PDE5 (IC_{50} = 5.9 µM); used to treat erectile dysfunction and has been shown to have anti-cancer and antioxidant activity; induces differentiation of cardiomyocytes and increases the proliferation and differentiation of cultured human osteoblasts

1 g
5 g
10 g
25 g



3-[(6-deoxy-α-L-mannopyranosyl)oxy]-7-(β-D-glucopyranosyloxy)-5-hydroxy-2-(4-methoxyphenyl)-8-(3-methyl-2-buten-1-yl)-4H-1-benzopyran-4-one

IGFBP5 Polyclonal Antibody 10008207

IBP-5, IGF-Binding Protein 5, Insulin-like Growth Factor Binding Protein 5
Supplied as: Peptide affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human IGFBP5 amino acids 192-206 • Host: rabbit • Cross Reactivity: (+) murine and rat IGFBP5 • Application(s): WB • IGFBP5 is a secreted protein that binds IGF-1 and restricts it from accessing its cell-surface receptor (IGF-1R). This aids in regulation of cell growth, differentiation, and apoptosis.

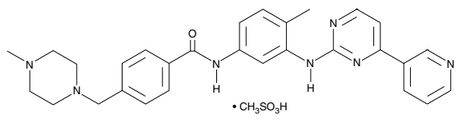
500 µl

• Also Available: **IGFBP5 Blocking Peptide** (10008206) 1 ea

Imatinib (mesylate) 13139

[220127-57-1] CGP57148B, Gleevec, Gilvec, STI-571
MF: $C_{29}H_{31}N_7O \bullet CH_4SO_3$ **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 (CML), gastrointestinal stromal tumors (GIST), 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

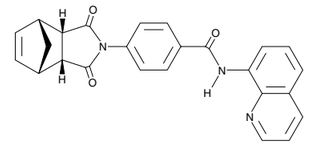


4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-methanesulfonate-benzamide

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



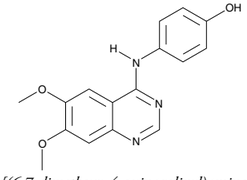
4-[(3aR,4S,7R,7aS)-1,3,3a,4,7,7a-hexahydro-1,3-dioxo-4,7-methano-2H-isoindol-2-yl]-N-8-quinolinyl-benzamide

• Also Available: **IWR-1-exo** (13598) 5 mg, 10 mg, 25 mg, 50 mg

Janex 1 10011246

[202475-60-3] WHI-P131
MF: $C_{16}H_{15}N_3O_3$ **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

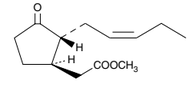


4-[(6,7-dimethoxy-4-quinazolinyl)amino]-phenol

(±)-Jasmonic Acid methyl ester 9000059

[39924-52-2] (±)-Methyl Jasmonate
MF: $C_{13}H_{20}O_3$ **FW:** 224.3 **Purity:** ≥95% (mixture of isomers)
A neat oil **Stability:** ≥1 year at -20°C
Summary: A mixture of *trans* (3R/7R and 3S/7S) isomers; induces the synthesis of proteinase inhibitors in plant leaves; in cancer cells, suppresses proliferation and induces apoptosis; inhibits hexokinase that is bound to mitochondria; methyl jasmonate derivatives also have potential as anti-inflammatory agents.

1 g
5 g
10 g
25 g



3-oxo-2-(2-penten-1-yl)-cyclopentaneacetic acid, methyl ester

vol. 11 Cn

Olivia May, Ph.D.

Phospholipase D Signaling in Cancer

Over the past several decades evidence for the involvement of phospholipids in cancer has been mounting. As a critical regulator of cell proliferation and survival, elevated PLD activity and overexpression has been implicated in multiple human cancers including breast, renal, gastric, thyroid, and colorectal. PLD activity is increased in response to mitogenic signals and activated oncoproteins, and its enzymatic product, phosphatidic acid (PA), can act as a tumor promoting second messenger that recruits critical signaling molecules to membranes. Inhibition of PLD enzymatic activity leads to increased cancer cell apoptosis, decreased cancer cell invasion, and decreased metastasis of cancer cells. Articulated below are some of the newer discoveries regarding PLD's role in cancer and the research tools being developed to further this understanding.

PLD, the Basics

PLD catalyzes the conversion of membrane phospholipids to the lipid second messenger PA and a polar head group.(Figure 1) Two mammalian isoforms of PLD have been characterized, PLD1 and PLD2. Structural similarities between the two isoforms are highlighted by 53% shared sequence identity, including the conserved phox consensus sequence (PX), pleckstrin homology (PH), and phosphatidylinositol and (4, 5) diphosphate (PIP_2) binding domains as well as the histidine, lysine, aspartate (HKD) catalytic sites. Despite these similarities, PLD1 and PLD2 are subject to different regulatory mechanisms with distinct patterns of expression. PLD1 has low basal activity that is highly regulated by protein kinase C (PKC) and the small GTPase proteins Arf and Rho, is localized to intracellular membranes, and participates in vesicle trafficking. PLD2 is constitutively active in many cell types and mediates a number of unique protein interactions when key tyrosine residues are phosphorylated in response to mitogens or growth factors. PLD2 was described originally as being localized to the plasma membrane, but subsequent studies have shown that PLD2 can have a cytosolic distribution. It is activated in intact cells by agonists binding to G-protein-coupled receptors and can be regulated by small GTP binding proteins, heterotrimeric GTP-binding proteins, and PKC isoforms. PLD1 can also be phosphorylated on tyrosine, but this modification has not been shown to lead to a significant change in activity. The distinct roles of the individual PLD isoforms remain to be fully delineated but are noted below when possible.

Tyrosine Phosphorylation of PLD2, Promoting Transformation

The enzymatic activity of PLD2 is complexly regulated by phosphorylation and dephosphorylation at specific activation and inhibitory sites. Recent *in vitro* studies report that at least three kinases, EGFR, JAK3, and Src are capable of phosphorylating PLD2 at tyrosine residues 296, 415, and 511, respectively.[1] (Figure 2) Upon phosphorylation, Y^{296} and Y^{415} have inhibitory and activational functions, respectively, the extent of which is context dependent. Phosphorylation of Y^{511} can yield either inhibition or activation depending on cell type. For example, COS-7 cells, which have high levels of PLD2 activity, are prominently phosphorylated by JAK3 on the Y^{415} activation site and moderately phosphorylated by EGFR kinase and Src on Y^{296} and Y^{511}, respectively. Conversely, in MCF-7 cells, an estrogen receptor positive, breast cancer cell type characterized by low PLD2 activity and delayed cell transformation, EGFR kinase prominently phosphorylates the Y^{296} inhibitory site of PLD2. Modest input from JAK3 at the Y^{415} activation site does not compensate for the negative modulation by EGFR kinase in MCF-7 cells, thus PLD2 activity is muted. Undoubtedly the interplay of phosphorylation on key tyrosine residues is cell-type specific as PLD2 can transform rat fibroblasts overexpressing c-Src or EGFR. Phosphatase activity at the inhibitory and activator sites of PLD2 also intricately regulates production of PA.

The phosphotyrosine motifs *p-YxN* at sites Y^{179} and Y^{511} on PLD2 additionally serve as docking sites for growth factor receptor bound protein 2 (Grb2).[2] When Grb2 is bound, PLD2-generated PA can recruit Sos, an activator of the Ras oncogene, to the plasma membrane. (Figure 2) Through activation of the Ras GTP/GDP exchange, PA is connected to downstream signaling of the Raf/MEK/ERK mitogen-activated protein kinase cascade, which is critical for cell proliferation/transformation.

PA Contributes to Cell Survival Through mTOR

Many of the oncogenic effects of PA can be attributed to its downsteam targets mTOR (mammalian target of rapaycin), a serine-threonine kinase that regulates cellular activities in response to environmental stress, and S6K1, the p70 ribosomal protein S6 kinase 1. Both mTOR complexes, mTORC1 and mTORC2, are dependent on PLD-derived PA for activation. (Figure 2) The raptor-associated mTORC1/S6K1 signaling

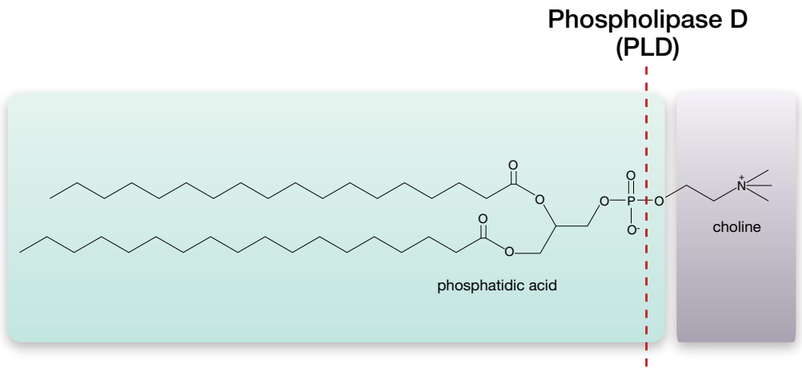


Figure 1. Phospholipase D hydrolyzes membrane phospholipids. For example, phosphatidylcholine is cleaved into phosphatidic acid and choline. Phosphatidic acid acts as a second messenger involved in intracellular protein trafficking, cytoskeleton organization, cell proliferation, and cancer cell transformation.

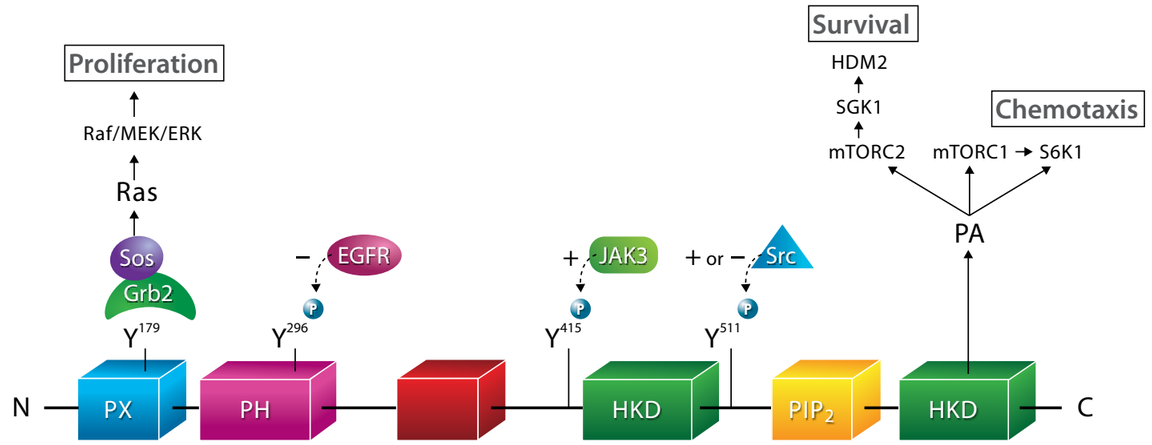


Figure 2. A protein map of PLD2 indicating the tyrosine phosphorylation targets discussed in this article. Recruitment of Grb2 and Sos connects PLD to the Raf/MEK/ERK signaling cascade. Phosphorylation by the kinases EGFR, JAK3, and Src has distinct inhibitory and/or activational activities on specific tryosine residues. The HKD catalytic domain of PLD enables production of PA, which becomes an important signaling component of the mTORC1, S6K1, and mTORC2 pathways.

cascade phosphorylates downstream targets involved in cell survival, cell migration, growth, and proliferation and thus, is most often associated with oncogenesis. As a negative feedback mechanism in the upstream direction, mTORC1 and S6K1 are capable of down-regulating levels of PLD2 gene expression. Whereas abnormally high levels of mTORC1 are thought to be an underlying cause in many cancers, elevated PLD activity signaling through mTORC2 and the serum- and glucocorticoid-inducible kinase 1 (SGK1) has been specifically shown to increase levels of human double minute 2 protein (HDM2), a p53 E3 ubiquitin ligase.[3] (Figure 2) When activated, HDM2 counters the pro-apoptotic signaling mediated by p53, thus further contributing to cancer cell survival.

PLD's Role in Cell Migration and Metastasis

PLD activity is important for cell mobility and migration. Overexpression of PLD2 can result in reorganization of the actin cytoskeleton, which plays a significant role in cell motility, whereas PLD2 knockdown leads to cell migration arrest. PA production through PLD activates mTOR/S6K (specifically S6K), which leads to actin polymerization and chemotaxis.[4] The association of Grb2 with PLD2 is capable of recruiting Wiskott-Aldrich syndrome protein (WASP) a protein that also potentiates actin polymerization.[4] Additionally, PLD-generated PA has been demonstrated to recruit DOCK2, the guanine nucleotide exchange factor of Rac1, to the leading edge of polarizing cells, resulting in increased actin polymerization.[4] Inappropriate cell motility accelerates the spread of cancer cells, and PLD activity has been implicated in tumor invasion. As one simple example, the ability of MDA-MB-231 human breast cancer cells (with high PLD activity) to migrate and invade a synthetic matrix is PLD dependent, unlike MCF-7 breast cancer cells, a low-invasive form of breast cancer with endogenously low PLD activity.[5] Invasive cancer cells also secrete proteases to promote metastasis. PLD activity has been correlated with increased protease secretion. Increased expression of PLD activity has been shown to stimulate secretion of a host of matrix metalloproteinases (MMPs) in a number of different cancer cells.[5]

Isoform-selective Inhibitors, New Hope for Treating Cancer

Original studies of PLD function widely relied on short-chain primary alcohols such as ethanol or *n*-butanol to competitively block phosphatidic acid production. These alcohols serve as competitive nucleophiles to water, resulting in a transphosphatidylation reaction that generates phosphatidylalcohol products instead of PA. Whereas phosphatidylalcohols are relatively inert and stable when incorporated into biological membranes and are useful for assaying PLD activity, they are indirect inhibitors of PA production and are not viable options for therapeutic use. With a burgeoning understanding of the role of PLD in cell proliferation, transformation, chemotaxis and metastasis, the availability of small-molecule, isoform-specific PLD inhibitors promises to help further define the respective roles of PLD1 and PLD2 and to potentially serve as a new approach for the treatment of cancer. For your research purposes, Cayman offers halopemide (Item No. 13205) and FIPI (Item No. 13563), both potent yet non-specific PLD inhibitors as well as CAY10593 (Item No. 13206) and CAY10594 (Item No. 13207), novel PLD1- and PLD2-specific inhibitors, respectively, designed and characterized by Dr. Alex Brown's group at Vanderbilt University.[5-7]

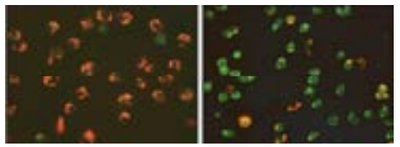
References

1. Henkels, K.M., Peng, H.-J., Frondorf, K., *et al. Mol. Cell. Biol.* **30(9)**, 2251-2263 (2010).
2. Henkels, K.M., Short, S., Peng, H.-J., *et al. Biochem. Biophys. Res. Commun.* **389(2)**, 224-228 (2009).
3. Lyo, D., Xu, L., and Foster, D.A. *Biochem. Biophys. Res. Commun.* **396**, 562-565 (2010).
4. Gomez-Cambronero, J. *Scientific World Journal* **10**, 1356-1369 (2010).
5. Su, W., Chen, Q., and Frohman, M.A. *Future Oncol.* **5(9)**, 1477-1486 (2009).
6. Su, W., Yeku, O., Olepu, S., *et al Mol. Pharmacol.* **75(3)**, 437-446 (2009).
7. Scott, S.A., Selvy, P.E., Buck, J.R., *et al. Nat. Chem. Biol.* **5(2)**, 108-117 (2009).

JC-1 Mitochondrial Membrane Potential Assay Kit 10009172

Stability: ≥6 months at -20°C
Summary: Mitochondrial membrane potential, Δψm, is an important parameter of mitochondrial function that is used as an indicator of cell health. JC-1 is a lipophilic, cationic dye that can selectively enter into mitochondria and reversibly change color from green to red as the membrane potential increases. In healthy cells with high mitochondrial Δψm, JC-1 spontaneously forms complexes known as J-aggregates with intense red fluorescence. On the other hand, in apoptotic or unhealthy cells with low Δψm, JC-1 remains in the monomeric form, which shows only green fluorescence. Cayman's JC-1 Mitochondrial Membrane Potential Assay provides all the necessary reagents, as well as complete instructions, for analysis of mitochondrial integrity in whole cells.

100 tests



Effect of staurosporine on mitochondrial potential in Jurkat cells. *Left Panel:* untreated cells show most of the cells had strong J-aggregation (red). *Right Panel:* staurosporine-treated cells show a majority of cells stained green due to low Δψm.

JMJD2A (human recombinant) 10336

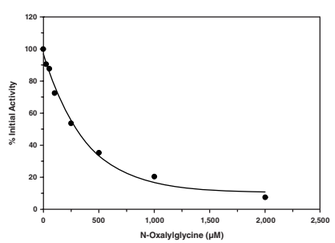
JHDM3A, Jumonji Domain Containing 2A, KDM4A, Lysine-Specific Demethylase 4A
Purity: ≥85%
Supplied in: 50 mM Hepes, pH 7.4, containing 150 mM sodium chloride and 20% glycerol **Stability:** ≥6 months at -80°C
Summary: Source: recombinant N-terminal His-tag protein expressed in *E. coli* • M_r: 43.0 kDa • JMJD2A catalyzes the demethylation of tri- and di-methylated forms of histone H3 at lysine residues 9 and 36. Its transcriptional function appears to depend on protein associations, as it is implicated in both transcriptional silencing and upregulation of the androgen receptor-dependent genes. The jumonji C domain-containing histone demethylases have been implicated in cancer cell growth and may be drug discovery targets for therapeutic intervention.

25 µg
50 µg
100 µg

JMJD2A Inhibitor Screening Assay Kit 700360

Jumonji Domain Containing 2A, KDM4A, Lysine-Specific Demethylase 4A
Stability: ≥6 months at -80°C
Summary: JMJD2A is a Jumonji C (JmjC) histone demethylase that catalyzes the demethylation of di- and trimethylated lysine 9 and lysine 36 of histone H3. Cayman's JMJD2A Inhibitor Screening Assay is based on the detection of formaldehyde produced during the demethylation of the trimethylated peptide substrate, histone H3 trimethyl lys9. Cyclization of formaldehyde and acetoacetanilide in the presence of ammonia gives a fluorescent product for quantitation.

96 wells



JMJD2A Polyclonal Antibody 10382

Jumonji Domain Containing 2A, KDM4A, Lysine-Specific Demethylase 4A
Supplied as: IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human recombinant JMJD2A amino acids 1-350 • Host: rabbit • Cross Reactivity: (+) human JMJD2A • Application(s): WB • JMJD2A is a lysine specific demethylase with emerging roles in histone modification or epigenetic remodeling.This JMJD2A polyclonal antibody was raised against an N-terminal recombinant fragment of JMJD2A. This fragment (amino acids 1-350) includes the JmjN and JmjC domains but not the two LAP/PHD zinc finger or Tudor domains of the 1,064 amino acid protein.

500 µl

JMJD2D (human recombinant) 10335

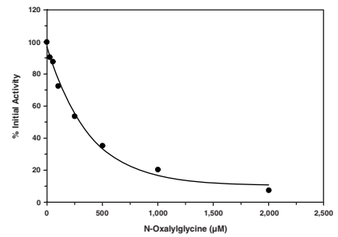
Jumonji Domain Containing 2D, KDM4D, Lysine-Specific Demethylase 4D
Purity: ≥95%
Supplied as: A solution in 50 mM Hepes, pH 7.4, containing 150 mM sodium chloride and 20% glycerol
Summary: Source: Human recombinant N-terminal His-tagged protein, expressed in *E. coli* • M_r: 42.7 kDa

25 µg
50 µg
100 µg

JMJD2D Inhibitor Screening Assay Kit 700370

Jumonji Domain Containing 2D, KDM4D, Lysine-Specific Demethylase 4D
Stability: ≥6 months at -80°C
Summary: Cayman's JMJD2D Inhibitor Screening Assay is based on the detection of formaldehyde produced during the demethylation of the trimethylated peptide substrate, histone H3 trimethyl lys9. Cyclization of formaldehyde and acetoacetanilide in the presence of ammonia gives a fluorescent product for quantitation.

96 wells



JMJD2D Polyclonal Antibody 10383

Jumonji Domain Containing 2D, KDM4D, Lysine-Specific Demethylase 4D
Supplied as: Antigen-affinity purified rabbit IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human recombinant JMJD2D amino acids 1-354 • Host: rabbit • Cross Reactivity: (+) human and murine JMJD2D • Application(s): FC, ICC, IP, and WB • JMJD2D is a lysine specific demethylase with emerging roles in histone modification or epigenetic remodeling. This JMJD2D polyclonal antibody was raised against an N-terminal recombinant fragment of JMJD2D.

500 µl

JMJD6 Peptide Affinity-Purified Polyclonal Antibody 13787

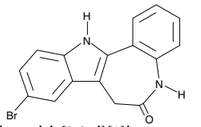
Jumonji Domain Containing 6, PTDSR
Supplied as: Antigen affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: synthetic peptide corresponding to human JMJD6 amino acids 127-144 • Host: rabbit • Cross Reactivity: (+) chimpanzee, ovine, canine, equine, human, murine, and opossum JMJD6 • Application(s): WB • JMJD6 is a 403 amino acid nuclear protein that acts as a bifunctional arginine demethylase and lysyl-hydroxylase. JMJD6 demethylates histone H3 at 'Arg-2' and histone H4 at 'Arg-3' and is known to function in the differentiation of multiple organs during embryogenesis, and regulate hematopoietic differentiation and macrophage cytokine responses.

1 ea

Kenpaullone 10010239

[142273-20-9] 9-Bromopaullone, NSC 664704
MF: $C_{16}H_{11}BrN_2O$ **FW:** 327.2 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An ATP-competitive inhibitor of several CDKs as well as GSK3β

1 mg
5 mg
10 mg
50 mg

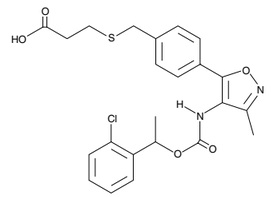


9-bromo-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one

Ki16425 10012659

[355025-24-0]
MF: $C_{23}H_{23}ClN_2O_5S$ **FW:** 475.0 **Purity:** ≥95%
A crystalline solid **Stability:** ≥1 year at -20°C
Summary: An LPA receptor antagonist with selectivity for LPA_1 and LPA_3; exhibits K_i values of 0.34, 6.5, and 0.93 µM for the human LPA_1, LPA_2, and LPA_3 receptors, respectively; at 10 µM, blocks LPA-induced cell migration of a variety of cancer cell lines

1 mg
5 mg
10 mg
100 mg



3-[[[4-[4-[[[1-(2-chlorophenyl)ethoxy]carbonyl]amino]-3-methyl-5-isoxazolyl]phenyl]methyl]thio]-propanoic acid

Kinase Screening Library (96-Well) 10505

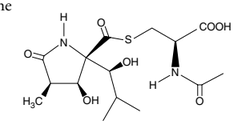
Supplied as: 10 mM solutions in DMSO
Summary: This screening plate includes 65 various kinase inhibitors.

100 µl

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

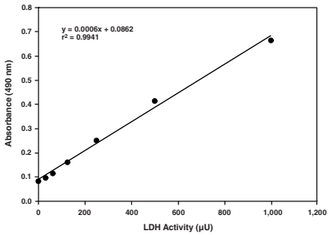


3S-hydroxy-2R-(1-hydroxy-2-methylpropyl)-4R-methyl-5-oxo-2-pyrrolidinecarboxylate-N-acetyl-L-cysteine

LDH Cytotoxicity Assay Kit 10008882

Lactate Dehydrogenase Cytotoxicity
Stability: ≥1 year at -20°C
Summary: LDH is a soluble cytosolic enzyme that is released into the culture medium following loss of membrane integrity resulting from either apoptosis or necrosis. LDH activity, therefore, can be used as an indicator of cell membrane integrity and serves as a general means to assess cytotoxicity resulting from chemical compounds or environmental toxic factors. Cayman's LDH Cytotoxicity Assay measures LDH activity present in culture medium using a coupled two-step reaction producing a highly-colored formazan dye which absorbs strongly at 490-520 nm.

96 wells
480 wells



15-Lipoxygenase-2 (human recombinant) 10011263

Arachidonate 15-LO Type II, 15-LOX-2
MF: Monomer **M_r:** 76 kDa **Purity:** ≥95%
Supplied as: A solution in PBS, pH 7.4, 1 mM DTT and 20% glycerol
Stability: ≥6 months at -80°C
Summary: Source: human recombinant C-terminal His-tagged protein expressed in *E. coli* • M_r: 76 kDa • 15-LO-2 oxygenates C15 of arachidonic acid to produce 15(S)-HETE. • Expression of 15-LO-2 appears to be restricted to prostate, lung, skin, and cornea and may play a role in the normal development of these tissues. 15-LO-2 is both down-regulated in prostate cancer compared with normal and benign prostate tissues, implicating a possible protective role for 15-LO-2 against tumor formation.

25 µg
50 µg
100 µg

15-Lipoxygenase-2 Polyclonal Antibody 10004454

Arachidonate 15-LO Type II, 15-LOX-2
Supplied as: Peptide affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human 15-LO-2 amino acids 161-179 • Host: rabbit • Cross Reactivity: (+) human 15-LO-2; (-) rabbit reticulocyte 15-LO-1 and porcine leukocyte 12-LO-1 • Application(s): WB • 15-LO-2 oxygenates C15 of arachidonic acid to produce 15(S)-HETE. Expression of 15-LO-2 appears to be restricted to prostate, lung, skin, and cornea and may play a role in the normal development of these tissues.

500 µl

• Also Available: **15-Lipoxygenase-2 Blocking Peptide** (10004457) 200 µg
15-Lipoxygenase-2 Western Ready Control (10011500) 1 ea

LSD Antibodies					
Item No.	**Item Name**	**Formulation**	**Host**	**Cross Reactivity**	**Application(s)**
13554	LSD1 Polyclonal Antibody (aa 100-150)	Peptide affinity-purified IgG	Rabbit	(+) Canine, human, murine, rat, Rhesus monkey, and zebrafish LSD1	WB
13553	LSD1 Polyclonal Antibody (aa 400-450)	Protein G-purified IgG	Rabbit	(+) Chimpanzee, bovine, canine, human, monkey, and murine LSD1	WB
13486	LSD1 Polyclonal Antibody (aa 450-500)	Protein A-purified IgG	Rabbit	(+) Chimpanzee, bovine, canine, equine, murine, orangutan, and porcine LSD1	WB
13555	LSD1 Polyclonal Antibody (aa 800-850)	Protein G-purified IgG	Rabbit	(+) Canine, human, murine, rat, and Rhesus monkey LSD1	IHC (paraffin-embedded sections) and WB

LSD1 (human recombinant) 10245

AOF2, BHC110, KDM1, Lysine-specific demethylase-1, NPAO, p110b

Supplied as: A solution in sodium phosphate, pH 7.2, containing 100 mM sodium chloride and 20% glycerol **Stability:** ≥6 months at -80°C

Summary: Source: human recombinant N-terminal His-tagged enzyme expressed in *E. coli*; BC048134 • M_r: 94 kDa • LSD1 is a component of several histone deacetylase co-repressor complexes including HDAC1 and 2, CtBP, and the neuronal CoREST complexes. LSD1, with the help of its cofactor CoREST, specifically demethylates mono- and dimethylated histone H3 lysine 4, resulting in transcriptional repression.

25 units
50 units
100 units

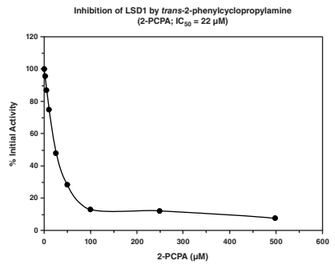
LSD1 Inhibitor Screening Assay Kit 700120

Lysine-Specific Demethylase 1

Stability: ≥6 months at -80°C

Summary: LSD1 is a histone demethylase whose actions on specific lysine residues alter transcription of chromosomal DNA. It also inhibits the tumor suppressor activity of p53 by demethylating a specific lysine residue. Cayman's LSD1 Inhibitor Screening Assay is based on a coupled enzymatic reaction in which LSD1 first produces H_2O_2 during the demethylation of lysine 4 of a histone 3 peptide. In the presence of horseradish peroxidase, H_2O_2 reacts with ADHP to produce the highly fluorescent compound resorufin. Sufficient human recombinant LSD1 is provided for 100 tests.

96 wells



LY294002 70920

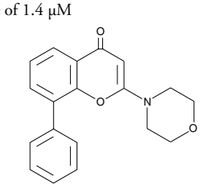
[154447-36-6]

MF: $C_{19}H_{17}NO_3$ **FW:** 307.3 **Purity:** ≥98%

A crystalline solid **Stability:** ≥1 year at -20°C

Summary: A selective PI3K inhibitor with 2.7-fold greater potency than quercetin; inhibits purified PI3K with an IC_{50} value of 1.4 µM

5 mg
10 mg
25 mg
50 mg



2-(4-morpholinyl)-8-phenyl-4H-1-benzopyran-4-one

LY364947 13341

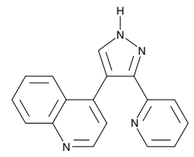
[396129-53-6] HTS 466284, TGF-β RI Kinase Inhibitor

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



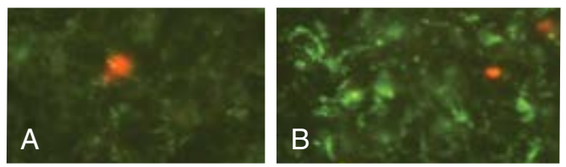
4-[3-(2-pyridinyl)-1H-pyrazol-4-yl]-quinoline

Lysosome/Cytotoxicity Dual Staining Kit 600310

Stability: ≥1 year at -20°C

Summary: Cayman's Lysosome/Cytotoxicity Dual Staining Kit is a tool for studying lysosome function at the cellular level. The kit employs 4-nitro-7-(1-piperazinyl)-2,1,3-benzoxadiazole (NBD-PZ), which is membrane permeable and reacts with carboxylic acids in the acidic luminal environment of lysosomes, as a probe for the detection of lysosomes in cultured cells. Propidium iodide is used as a marker of cell death. Chloroquine, a known inhibitor of lysosome function, is included as a positive control. The kit provides sufficient reagents to effectively treat/stain up to 10 plates worth of cells irrespective of the number of wells/plate.

1 ea



Chloroquine increases lysosome accumulation but not cell death in HepG2 cells as measured by fluorescent microscopy. *Panel A:* HepG2 cells treated with vehicle. There was a basal level of lysosome staining, indicated by faint green staining of NBD-PZ. Few dead cells were detected (red nuclei staining by propidium iodide). *Panel B:* HepG2 cells treated with 12.5 µM chloroquine. Note the increase in NBD-PZ fluorescence intensity but not the number of propidium iodide positive dead cells compared to the cells treated with vehicle.

M 344 13174

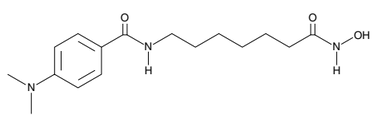
[251456-60-7] D237, Histone Deacetylase Inhibitor III, MS 344

MF: $C_{16}H_{25}N_3O_3$ **FW:** 307.4 **Purity:** ≥98%

A crystalline solid **Stability:** ≥2 years at -20°C

Summary: An inhibitor of HDACs, inhibiting maize HDAC (IC_{50} = 100 nM) as well as human HDAC1 (IC_{50} = 46 nM); shows a 3-fold selectivity for HDAC6 over HDAC1

5 mg
10 mg
25 mg
50 mg



4-(dimethylamino)-N-[7-(hydroxyamino)-7-oxoheptyl]-benzamide

2-thio-Acetyl MAGE 10009651

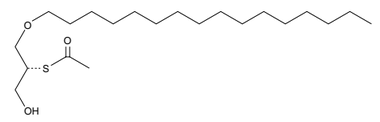
[112014-15-0] 2-thioacetyl Monoacylglycerol ether

MF: $C_{21}H_{42}O_3S$ **FW:** 374.6 **Purity:** ≥97%

A solution in methyl acetate **Stability:** ≥1 year at -80°C

Summary: A colorimetric substrate for KIAA1363, a 2-acetyl monoacylglyceryl ether hydrolase critical to the survival and proliferation of many cancer cell lines

1 mg
5 mg
10 mg
25 mg



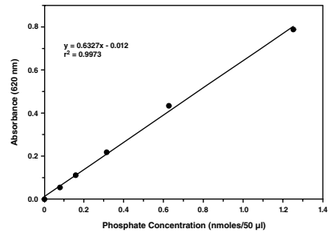
S-[2-(hexadecyloxy)-1-(hydroxymethyl)ethyl]ester, ethanethioic acid

Malachite Green Phosphate Assay Kit 10009325

Stability: ≥6 months at 4°C

Summary: Cayman's Malachite Green Phosphate Assay provides a fast, reproducible, colorimetric method for measuring inorganic free phosphate in aqueous solutions. Applications for this assay include quantification of phosphorylation and phosphate release from protein phosphatase substrates. The assay is formatted to a 96-well plate, but could easily be modified for use in 384-well or cuvette-based assays.

96 wells



Mammalian STE-20-Like Kinase 1 Polyclonal Antibody 13776

KRS2, MST-1, STK4

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

Summary: Antigen: synthetic peptide from 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, upon cleavage, has been implicated in the promotion of chromatin condensation. The C-terminus of MST-1 contains two functional nuclear export signals, which are released upon caspase-mediated cleavage. The N-terminus portion of the protein then translocates to the nucleus and promotes chromatin condensation at sufficiently high levels. Full-length MST-1 is localized to the cytoplasm.

1 ea

Manumycin A 10010497

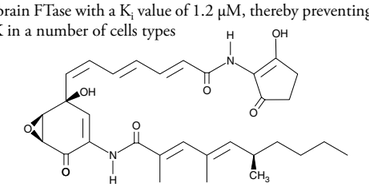
[52665-74-4] NSC 622141, UCF 1C

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 farnesyltransferase (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 a number of cells types

500 µg
1 mg
5 mg
10 mg



N-[(1S,5S,6R)-5-hydroxy-5-[(1E,3E,5E)-7-[(2-hydroxy-5-oxo-1-cyclopenten-1-yl) amino]-7-oxo-1,3,5-heptatrien-1-yl]-2-oxo-7-oxabicyclo[4.1.0]hept-3-en-3-yl]-2E,4E,6R-trimethyl-2,4-decadienamide

D-*erythro*-MAPP 10165

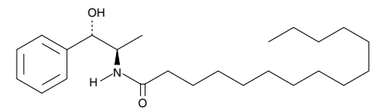
[143492-38-0] (1S,2R-D-erythro-2-N-myristoylamino)-1-phenyl-1-propanol

MF: $C_{23}H_{29}NO_2$ **FW:** 361.6 **Purity:** ≥98%

A crystalline solid **Stability:** ≥1 year at -20°C

Summary: An analog of ceramide that inhibits alkaline ceramidase (IC_{50} ~5 µM); suppresses growth of HL-60 cancer cells in culture

500 µg
1 mg
5 mg
10 mg



N-[(1R,2S)-2-hydroxy-1-methyl-2-phenylethyl]-tetradecanamide

Maslinic Acid 10009645

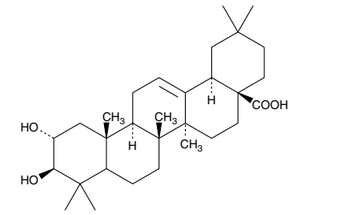
[4373-41-5] Crategolic Acid, 2α-Hydroxyoleanoic Acid

MF: $C_{30}H_{48}O_4$ **FW:** 472.7 **Purity:** ≥98%

A crystalline solid **Stability:** ≥2 years at -20°C

Summary: An antiproliferative agent against Caco-2 cancer cells (EC_{50} = 15 µM), HT-29 human colon cancer cells (EC_{50} = 74 µM), 1321N1 astrocytoma cells (IC_{50} = 25 µM), and human leukemia (CCRF-CEM and CEM/ADR5000) cells (IC_{50} = 7 and 9 µM respectively)

1 mg
5 mg
10 mg
25 mg



2α,3β-dihydroxy-olean-12-en-28-oic acid

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

Suppled as: 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, murine, 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

Suppled as: Affinity-purified IgG **Stability:** ≥1 year at -20°C

Summary: Antigen: phosphopeptide corresponding to amino acid residues surrounding phospho-Thr^{386} of human MEK1; expected to react with bovine, human, murine, non-human primates, and *Xenopus* MEK1 • Host: rabbit • 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 (Phospho-Ser^{218,222}) Polyclonal Antibody 10009178

Supplied as: 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

Metastasis Associated 1 Family Member 2 Polyclonal Antibody 13778

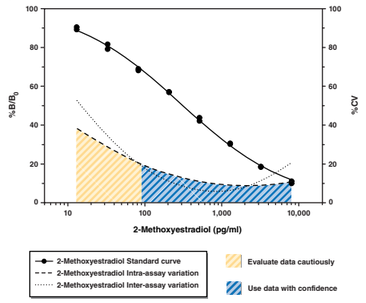
MTA2, MTA-L1 Protein, p53 Target Protein in Deacetylase Complex, PID
Supplied as: Antigen affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: synthetic peptide from a portion of human MTA2 amino acids 650-700 • Host: rabbit • Cross Reactivity: (+) chimpanzee, human, and Rhesus monkey MTA2 • Application(s): IHC and WB • MTA2 is a nuclear protein that interacts with HDAC1 and HDAC2 and has a functional role in chromatin remodeling and deacetylase activity. It interacts with p53 and represses p53-dependent transcriptional activation, thereby regulating p53-mediated cell growth arrest and apoptosis.

1 ea

2-Methoxyestradiol EIA Kit 582261

2-Hydroxyestradiol 2-methyl ester, 2-ME2
Stability: ≥1 year at -20°C
Sensitivity: 50% B/B_0: 350 pg/ml • 80% B/B_0: 40 pg/ml
Summary: 2-ME2 is a natural metabolite of estradiol with potent antitumor and antiangiogenic properties. Cayman's 2-Methoxyestradiol EIA is a competitive assay that can be used for quantification of 2-ME2 in plasma, urine, and other sample matrices.

96 strip/solid wells
480 strip/solid wells



Methylated Lysine Polyclonal Antibody 13727

Suppled as: Affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: methylated KLH • Host: rabbit • Cross Reactivity: (+) methylated lysine residues • Application(s): ELISA, IHC, IP and WB • Lysine can be methylated once, twice, or three times by lysine methyltransferases. The transfer of methyl groups from SAM to histones is catalyzed by histone methyltransferases.

400 µl

Methylated Lysine Polyclonal Antibody-biotin 13728

Supplied as: Affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: methylated KLH • Host: rabbit • Cross Reactivity: (+) methylated lysine residues • Application(s): ELISA, IP, and WB • Lysine can be methylated once, twice, or three times by lysine methyltransferases. The transfer of methyl groups from SAM to histones is catalyzed by histone methyltransferases.

400 µl

Methylated Lysine Polyclonal Antibody HRP Conjugate 13729

Supplied as: Affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: methylated KLH • Host: rabbit • Cross Reactivity: (+) multi-species • Application(s): ELISA and WB • Lysine can be methylated once, twice, or three times by lysine methyltransferases. The transfer of methyl groups from SAM to histones is catalyzed by histone methyltransferases.

400 µl

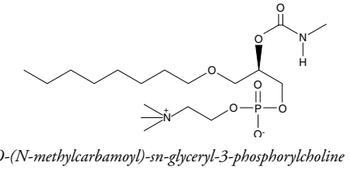
Phosphatidylinositols

Item No.	Item Name
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)
10008396	PtdIns-(3,5)-P_2 (1,2-dihexanoyl) (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)
10007764	PtdIns-(3,4,5)-P_3 (1,2-dioctanoyl) (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)
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)
64920	PtdIns-(3,4,5)-P_3 (1,2-dipalmitoyl) (sodium salt)
10008398	PtdIns-(3,5)-P_2 (1,2-dipalmitoyl) (sodium salt)
64923	PtdIns-(4)-P_1 (1,2-dipalmitoyl) (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-dipalmitoyl)-d_{62} (sodium salt)
64925	PtdIns-(5)-P_1 (1,2-dipalmitoyl) (ammonium salt)
10009817	PtdIns-(3,4,5)-P_3 Binding Protein
64930	PtdIns-(3,4,5)-P_3 (1-stearoyl, 2-arachidonoyl) (sodium salt)
10009241	PtdIns-(4)-P_1 Binding Protein
10010181	Ptd(S)Ins-(3,4)-P_2 (1,2-dioctanoyl) (sodium salt)
10010112	Ptd(S)Ins-(3,4)-P_2 (1,2-dipalmitoyl) (sodium salt)

Methylcarbamyl PAF C-8 9000332

MF: $C_{18}H_{39}N_2O_7P$ **FW:** 426.5 **Purity:** ≥98%
A solution in ethanol **Stability:** ≥1 year at -20°C
Summary: A C-8 analog of methylcarbamyl PAF C-16, a stable analog of PAF C-16 with a half-life greater than 100 minutes in platelet poor plasma; induces G_1-phase cell cycle arrest, suggesting a potential role in the inhibition of oncogenic transformation

1 mg
5 mg
10 mg
25 mg



1-O-octyl-2-O-(N-methylcarbamoyl)-sn-glyceryl-3-phosphorylcholine

Methyl-CpG-Binding Domain 1 Monoclonal Antibody (Clone 100B272.1) 13771

MBD1
Supplied as: Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: synthetic peptide corresponding to human MBD1 amino acids 391-405 • Host: mouse, clone 100B272.1 • Isotype: IgG_1 • Cross Reactivity: (+) human MBD1 • Application(s): WB • DNA methylation, or the addition of methyl groups to cytosine bases in the dinucleotide CpG, is imperative to proper development and regulates gene expression. The methylation pattern involves the enzymatic processes of methylation and demethylation associated with a MBD. MeCP2 and MBD1 (PCM1) repress transcription by binding specifically to methylated DNA.

1 ea

Methyl-CpG-Binding Domain 1 Polyclonal Antibody 13772

MBD1
Supplied as: Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: mixture of synthetic peptides corresponding to amino acids 98-113 and 391-405 of human MBD1 • Host: rabbit • Cross Reactivity: (+) human MBD1 • Application(s): WB • DNA methylation plays an essential role in mammalian development. MBD1 contains an MBD that allows it to bind specifically to methylated DNA and to repress transcription from methylated gene promoters.

1 ea

Methyl-CpG-Binding Domain 2-Binding Zinc Finger Polyclonal Antibody 13777

HINFP, Histone H4 Transcription Factor, MBD2-Binding Zinc Finger, MIZF
Supplied as: Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: a mixture of synthetic peptides corresponding to amino acids 180-194, 331-346, and 371-388 of human MIZF • Host: rabbit • Cross Reactivity: (+) human MIZF • Application(s): WB • MIZF protein represses transcription by associating with MBD2 in a histone deacetylase complex.

1 ea

Methyl-CpG-Binding Protein 2 Polyclonal Antibody 13775

MeCP2
Supplied as: Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: a mixture of synthetic peptides corresponding to amino acids 11-25 and 181-195 of human MeCP2 • Host: rabbit • Cross Reactivity: (+) human MeCP2 • Application(s): WB • MeCP2 may function as a mediator of the biological consequences of the methylation signal. It is also reported that this protein functions as a demethylase to activate transcription, as DNA methylation causes gene silencing.

1 ea

Methyl-CpG-Binding Domain 2/3 Monoclonal Antibody (Clone 106B691) 13773

MBD2, MBD3
Supplied as: Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: synthetic peptide corresponding to human MBD3 amino acids 215-230 • Host: mouse, clone 106B691 • Isotype: $IgG_{1κ}$ • Cross Reactivity: (+) human MBD2/3; also predicted to detect murine and rat MBD2/3 • Application(s): WB • MBD2 and MBD3 are members of a family of nuclear proteins related by the presence in each of a methyl binding domain. MBD2 is capable of binding specifically to methylated DNA, whereas MBD3 cannot.

1 ea

Methyl-CpG-Binding Domain 4 Polyclonal Antibody 13774

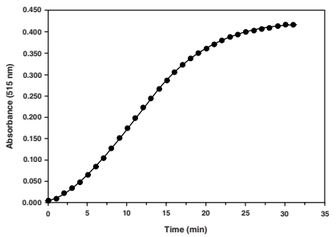
MBD4
Supplied as: Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: a mixture of synthetic peptides corresponding to amino acids 268-282 and 337-352 of human MBD4 • Host: rabbit • Cross Reactivity: (+) human MBD4 • Application(s): ICC, IHC, and WB • MBD4 binds specifically to methylated DNA. It has homology to bacterial base excision repair DNA N-glycosylases/lyases.

1 ea

Methyltransferase Colorimetric Assay Kit 700140

MT
Stability: ≥6 months at -80°C
Summary: Cayman's MT Colorimetric Assay is a continuous enzyme-coupled assay that can continuously monitor SAM-dependent MT activities. The removal of the methyl group from SAM generates AdoHcy, which is rapidly converted to urate and H_2O_2 by an enzyme mixture provided in the kit. H_2O_2 is measured with the colorimetric reagent 3,5-dichloro-2-hydroxybenzenesulfonic acid. The assay can be used with any SAM-dependent MT.

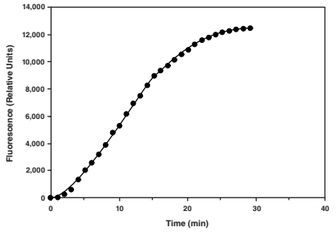
96 wells



Methyltransferase Fluorometric Assay Kit 700150

MT
Stability: ≥6 months at -80°C
Summary: Cayman's MT Fluorometric Assay is a continuous enzyme-coupled assay that can continuously monitor SAM-dependent MTs. The removal of the methyl group from SAM generates AdoHcy, which is rapidly converted to urate and H_2O_2 by an enzyme mixture provided in the kit. The reaction between H_2O_2 and ADHP produces the highly fluorescent compound resorufin. The assay can be used with any purified SAM-dependent MT.

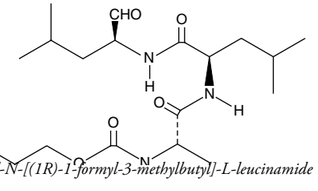
96 wells



(R)-MG132 13697

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



N-[(phenylmethoxy)carbonyl]-L-leucyl-N-[(1R)-1-formyl-3-methylbutyl]-L-leucinamide

• Also Available: **(S)-MG132** (10012628)

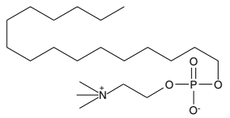
1 mg
5 mg
10 mg
50 mg

Miltefosine 63280

[58066-85-6] HePC

MF: $C_{21}H_{46}NO_4P$ **FW:** 407.6 **Purity:** ≥98%
A crystalline solid **Stability:** ≥1 year at -20°C
Summary: An inhibitor of CTP:phosphocholine cytidylyl transferase with antimetastatic properties

25 mg
50 mg
100 mg
500 mg

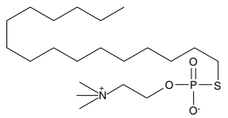


1-hexadecylphosphorylcholine

thio-Miltefosine 10009813

MF: $C_{21}H_{46}NO_3PS$ **FW:** 423.6 **Purity:** ≥98%
A neat oil **Stability:** ≥1 year at -20°C
Summary: A sulfur-containing derivative of miltefosine; the pharmacology of thio-miltefosine has not been published

1 mg
5 mg
10 mg
25 mg



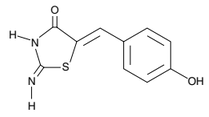
1-hexadecyl-thio-phosphorylcholine

Mirin 13208

[299953-00-7]

MF: $C_{10}H_8N_2O_2S$ **FW:** 220.3 **Purity:** ≥95%
An orange crystalline solid **Stability:** ≥2 years at -20°C
Summary: An inhibitor of the DNA damage sensor MRN, inhibiting MRN-dependent phosphorylation of histone H2AX (IC_{50} = 66 µM); prevents activation of ATM by blocking the nuclease activity of Mre11; induces G_2 arrest, abolishes the radiation-induced G_2/M checkpoint, and prevents homology-directed repair of DNA damage

5 mg
10 mg
50 mg
100 mg



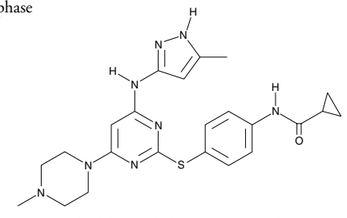
2-amino-5-[(4-hydroxyphenyl)methylene]-4(5H)-thiazolone

MK 0457 13600

[639089-54-6] Tozasertib, VX 680

MF: $C_{23}H_{28}N_8OS$ **FW:** 464.6 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent pan-Aurora kinase inhibitor that favors Aurora A (K_i = 0.6 nM) over Aurora B (K_i = 18 nM) or Aurora C (K_i = 4.6 nM); inhibits proliferation of clear cell renal carcinoma (IC_{50} <10 µM), inhibits histone H3 phosphorylation, and increases apoptosis; disrupts bipolar spindle formation during mitosis, arresting cell cycle progression at the G_2/M phase

25 mg
50 mg
100 mg
250 mg



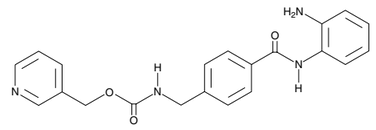
N-[4-[[4-(4-methyl-1-piperazinyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]-cyclopropanecarboxamide

MS-275 13284

[209783-80-2] Entinostat, SNDX 275

MF: $C_{21}H_{20}N_4O_3$ **FW:** 376.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An inhibitor of HDACs that preferentially inhibits HDAC1 (IC_{50} = 300 nM) over HDAC3 (IC_{50} = 8 µM); does not inhibit HDAC8; induces p21/CIP1/WAF1, slowing cell growth, differentiation, and tumor development *in vivo*

1 mg
5 mg
10 mg
25 mg

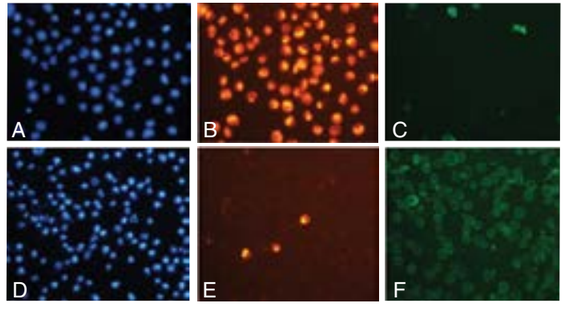


N-[[4-[[(2-aminophenyl)amino]carbonyl]phenyl]methyl]-3-pyridinylmethyl ester, carbamic acid

Multi-Parameter Apoptosis Assay Kit 600330

Stability: ≥1 year at -20°C
Summary: Cellular events in apoptosis include loss of cell membrane asymmetry, cell shrinkage, membrane blebbing, nuclear fragmentation, and chromatin condensation. Cayman's Multi-Parameter Apoptosis Assay includes four different reagents for monitoring several events in apoptosis. It employs FITC-conjugated Annexin V as a probe for phosphatidylserine on the outer membrane of apoptotic cells, TMRE as a probe for mitochondrial membrane potential, 7-AAD as an indicator of membrane permeability/cell viability, and Hoechst Dye to demonstrate nuclear morphology. The kit allows phenotypic characterization of different cell death parameters at a single-cell level. The assay can be adapted to high content screening with appropriate equipment. The reagents provided in the kit are sufficient to run 100 samples when using flow cytometry or 500 samples when using a 96-well plate format.

5 x 96 wells



Staurosporine induces apoptosis in Jurkat cells, as measured by nuclear morphology, a decrease in mitochondrial membrane potential, and an increase of Annexin V FITC positive cells. Jurkat cells were plated at a density of 5 x 10^4 cells/well in a 6-well plate. The next day, cells were treated with vehicle (control; A-C) or 2.5 µg/ml staurosporine (treatment; D-F) for five hours. Hoechst staining shows that most control cells have round and intact nuclei (*Panel A*) whereas staurosphorine-treated cells mostly have condensed and fragmented nuclei (*Panel D*). TMRE staining reveals that most control cells have undisrupted mitochondrial membrane potential (*Panel B*) whereas staurosporine-treated cells mostly have diminished membrane potential and were not stained (*Panel E*). Most control cells are Annexin V negative (*Panel C*) whereas cells treated with staurosporine are mostly Annexin V postiive (*Panel F*), indicating cells are undergoing apoptosis.

MutL Protein Homolog 1 Monoclonal Antibody (Clone 164C819) 13779

HNPCC, MLH1

Supplied as: Protein G-purified IgG **Stability:** ≥6 months at 4°C
Summary: Antigen: synthetic peptide from human MLH1 amino acids 387-403 • Host: mouse, clone 164C819 • Isotype: $IgG_{1κ}$ • Cross Reactivity: (+) human MLH1 • Application(s): WB • Human MutL Homologue (hMLH1) is homologous to the bacterial DNA mismatch repair mutL gene. Mutations in the hMLH1 gene are associated with hereditary non-polyposis colon cancer and various other cancers.

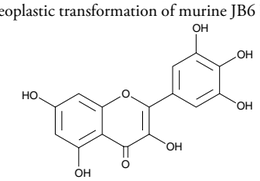
1 ea

Myricetin 10012600

[529-44-2] Cannabiscetin, NSC 407290

MF: $C_{15}H_{10}O_8$ **FW:** 318.2 **Purity:** ≥98%
A crystalline solid **Stability:** ≥1 year at -20°C
Summary: A flavonoid compound that acts as a powerful antioxidant; inhibits TBARS formation with an IC_{50} value of 6.34 µM; blocks oxLDL uptake by U937-derived macrophages at 20 µM; demonstrates potent chemopreventative potential by binding JAK1/STAT3 to inhibit neoplastic transformation of murine JB6 P^+ cells

10 mg
25 mg
50 mg
100 mg



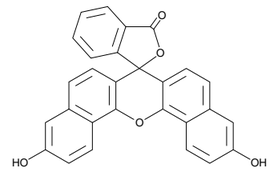
3,5,7-trihydroxy-2-(3,4,5-trihydroxyphenyl)-4H-1-benzopyran-4-one

Naphthofluorescein 13055

[61419-02-1] CCG 8295

MF: $C_{28}H_{16}O_5$ **FW:** 432.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A cell-permeable inhibitor of furin (IC_{50} = 12 µM); inhibits furin-mediated cleavage of the pro-form of membrane type-1 matrix metalloproteinase MT1-MMP, resulting in decreased levels of active MT1-MMP; inhibits the invasion of Matrigel by the human fibrosarcoma cell line HT1080

1 mg
5 mg
10 mg
50 mg

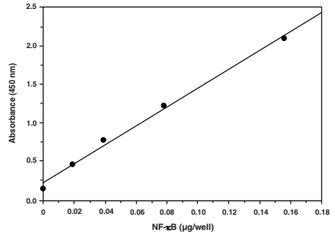


3,11-dihydroxy-spiro[7H-dibenzo[c,h]xanthene-7,1'(3'H)-isobenzofuran]-3'-one

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

Stability: ≥6 months at -20°C
Summary: Cayman's NF-κB (human p50) Transcription Factor Assay is a non-radioactive, sensitive mehod for detecting specific transcription factor DNA binding activity in nuclear extracts and whole cell lysates in a 96-well ELISA format. Cayman's NF-κB (human p50) Transcription Factor Assay detects NF-κB (p50). It will not cross-react with NF-κB (p65).

96 wells

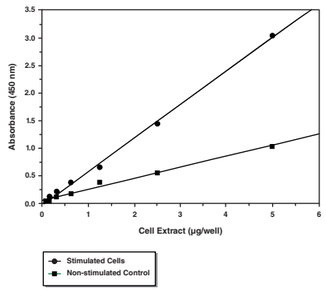


• Also Available: **NF-κB (human p50/p65) Combo Transcription Factor Assay Kit** (10011223) 96 wells

NF-κB (p65) Transcription Factor Assay Kit 10007889

Stability: ≥6 months at -20°C
Summary: Cayman's NF-κB (p65) Transcription Factor Assay detects human NF-κB (p65). It will not cross-react with NF-κB (p50).

96 wells



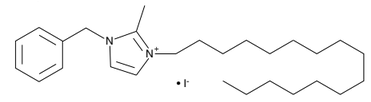
• Also Available: **NF-κB (human p50/p65) Combo Transcription Factor Assay Kit** (10011223) 96 wells

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 IC_{50} values ranging from 0.7-4.7 µM; decreases 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



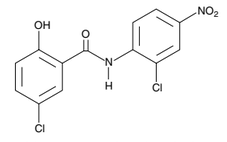
1-hexadecyl-2-methyl-3-(phenylmethyl)-1H-imidazolium-iodide

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 that has been used safely in humans for over 50 years; 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



5-chloro-N-(2-chloro-4-nitrophenyl)-2-hydroxy-benzamide

Nilotinib 10010422

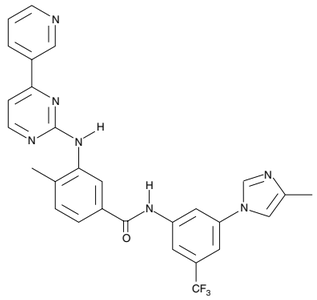
[641571-10-0] AMN107

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); regulates the expression of DNA helicase complex, cyclins, and cyclin-dependent kinases, inhibiting cell proliferation

5 mg
10 mg
25 mg
50 mg



4-methyl-N-[3-(4-methyl-1H-imidazol-1-yl)-5-(trifluoromethyl)phenyl]-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]-benzamide

S-Nitrosylated Protein Detection Kit 10006518

Stability: ≥1 year at -20°C

Summary: Cayman's S-Nitrosylated Protein Detection Assay employs a modification of the Jaffrey, *et al.* 'Biotin-switch' method to allow for the direct visualization of S-nitrosylated proteins in whole cells or tissues, as well as by overlay blotting analysis. Using this method, free SH groups are first blocked and any S-NO bonds present in the sample are then cleaved. Biotinylation of the newly formed SH groups provides the basis for visualization using streptavidin-based colorimetric or fluorescence detection.

1 ea

Nodularin 10007190

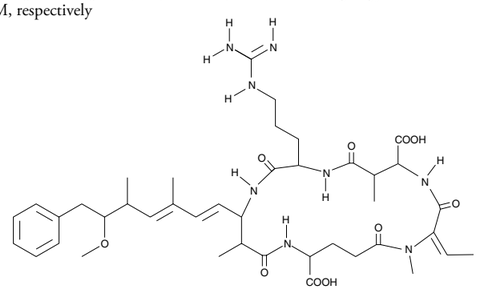
[118399-22-7]

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 monocyclic 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



cyclo[3S-amino-9S-methoxy-2S,6E,8S-trimethyl-10-phenyl-4,6-decadienoyl-D-γ-glutamyl-(2Z)-2-(methylamino)-2-butenoyl-(3S)-3-methyl-D-β-aspartyl-L-arginyl]

tetramethyl Nordihydroguaiaretic Acid 70302

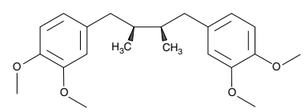
[24150-24-1] EM-1421, M4N, Terameprocol, tetramethyl NDGA, TMNDGA

MF: $C_{22}H_{30}O_4$ **FW:** 358.5 **Purity:** ≥98%

A crystalline solid **Stability:** ≥2 years at -20°C

Summary: A synthetic derivative of NDGA, a non-selective LO inhibitor; inhibits Sp1 transcription factor binding at the HIV long terminal repeat promoter and at the α-ICP4 promoter, a gene essential for HSV replication, with IC_{50} values of 11 and 43.5 µM, respectively; has antitumorigenic activity inducing growth arrest and apoptosis

50 mg
100 mg
500 mg
1 g



[(2R,3S)-4-(3,4-dimethoxyphenyl)-2,3-dimethylbutyl]-1,2-dimethoxy-benzene

NSC 23766 (hydrochloride) 13196

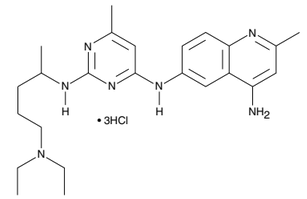
[1177865-17-6]

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 guanine nucleotide exchange factors 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



N6-[2-[[4-(diethylamino)-1-methylbutyl]amino]-6-methyl-4-pyrimidinyl]-2-methyl-4,6-quinolinediamine, trihydrochloride

NSC 210902 10011255

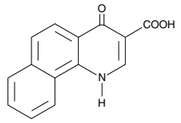
[51726-83-1]

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
25 mg



1,4-dihydro-4-oxo-benzo[h]quinoline-3-carboxylic acid

NSC 663284 13303

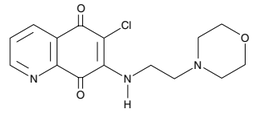
[383907-43-5] Cdc25 Phosphatase Inhibitor II, DA-3003-1

MF: $C_{15}H_{16}ClN_3O_3$ **FW:** 321.8 **Purity:** ≥98%

A crystalline solid **Stability:** ≥2 years at -20°C

Summary: A potent, cell-permeable, and irreversible inhibitor of all Cdc25 isoforms, with preference for Cdc25A (IC_{50} = 29, 95, and 89 nM for Cdc25A, Cdc25B2, and Cdc25C, respectively); arrests cells at both G_1 and G_2/M phases and prevents the proliferation of several human tumor cell lines

1 mg
5 mg
10 mg
50 mg



6-chloro-7-[[2-(4-morpholinyl)ethyl]amino]-5,8-quinolinedione

NU 7026 13308

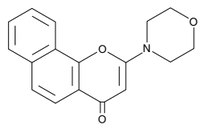
[154447-35-5] DNA-PK Inhibitor II, LY293646

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



2-(4-morpholinyl)-4H-naphtho[1,2-b]pyran-4-one

(±)-Nutlin-3 10004372

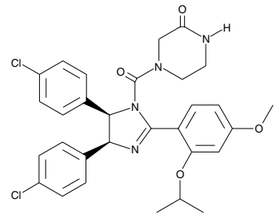
[548472-68-0] *Sold under license from Hoffman-La Roche*

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 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



(±)-4-[4,5-bis-(4-chlorophenyl)-2-(2-isopropoxy-4-methoxy-phenyl)-4,5-dihydro-imidazole-1-carbonyl]-piperazin-2-one

(-)-Nutlin-3 18585

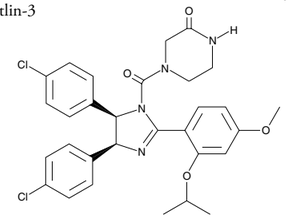
Nutlin 3a *Sold under license from Hoffman-La Roche*

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



(-)-4-(4,5-bis(4-chlorophenyl)-2-(2-isopropoxy-4-methoxyphenyl)-4,5-dihydro-1H-imidazole-1-carbonyl)piperazin-2-one

• Also Available: **(+)-Nutlin-3** (10009816) 1 mg, 5 mg, 10 mg, 25 mg

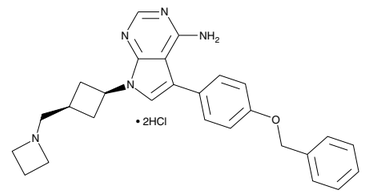
NVP-AEW541 (hydrochloride) 13641

MF: $C_{27}H_{29}N_5O$ • 2HCl **FW:** 512.5 **Purity:** ≥98%

A crystalline solid **Stability:** ≥2 years at -20°C

Summary: A selective IGF-1R kinase inhibitor (IC_{50} = 0.086 µM); prevents IGF-1-mediated survival and proliferation of MCF-7 cells (IC_{50} = 0.16 and 1.64 µM, respectively); dose-dependently inhibits tumor growth in a murine NWT-21 fibrosarcoma tumor model

500 µg
1 mg
5 mg
10 mg



7-[cis-3-(1-azetidinylmethyl)cyclobutyl]-5-[3-(phenylmethoxy)phenyl]-7H-pyrrolo[2,3-d]pyrimidin-4-amine, dihydrochloride

NVP-BEZ235 10565

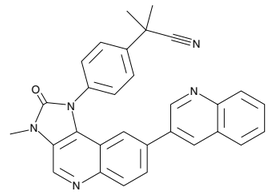
[915019-65-7] BEZ235

MF: $C_{30}H_{23}N_5O$ **FW:** 469.5 **Purity:** ≥98%

A crystalline solid **Stability:** ≥2 years at -20°C

Summary: A potent dual inhibitor of PI3K and mTOR that is well tolerated, displays disease stasis when administered orally, and enhances the efficacy of other anti-cancer agents when used in *in vivo* combination studies; inhibits PI3K isoforms and mutants with low nanomolar IC_{50} values; directly blocks cell growth and indirectly inhibits angiogenesis

25 mg
50 mg
100 mg
250 mg



4-[2,3-dihydro-3-methyl-2-oxo-8-(3-quinolinyl)-1H-imidazo[4,5-c]quinolin-1-yl]-α,α-dimethyl-benzeneacetonitrile

9(Z),11(E),13(E)-Octadecatrienoic Acid 10008349

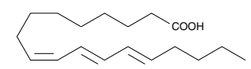
[506-23-0] α-Eleostearic Acid, α-ESA

MF: $C_{18}H_{30}O_2$ **FW:** 278.4 **Purity:** ≥98%

A crystalline solid **Stability:** ≥1 year at -80°C

Summary: A conjugated PUFA commonly found in plant seed oil; induces apoptosis and suppresses growth

1 mg
5 mg
10 mg
50 mg



9Z,11E,13E-octadecatrienoic acid

• Also Available: **9(Z),11(E),13(E)-Octadecatrienoic Acid ethyl ester** (10008350) 1 mg, 5 mg, 10 mg, 50 mg

vol. 11 Cn

Thomas G. Brock, Ph.D.

Infections in Cancer

Genetics, genomes, and even epigenetics are hot topics at cancer conferences this year. Popular in recent years, but still in the list of major symposia and mini-conferences, are molecular pathways, stem cells, and the microenvironment of the tumor. It might be easy to forget the central role that infectious agents play in causing cancer, given their disappearance from center stage at major conferences. Is there less interest in pathogens as oncogens? A quick look at PubMed reveals that, in 2009, there were almost 200 epigenetics/cancer publications and some 2,750 stem cell/cancer papers. The same year, there were over 4,500 papers on viruses/cancer! Moreover, interest in viruses is increasing. A more thorough look through PubMed shows a nice steady rise over time in virus/cancer reports (Figure 1). Not only has the publication rate continued to climb over a 5 decade period, but it's even more impressive that it's still rising after reaching 4,000 a decade back. Moreover, it is now clear that some bacteria can cause cancer. Certainly, the role of infections in cancer deserves a closer look.

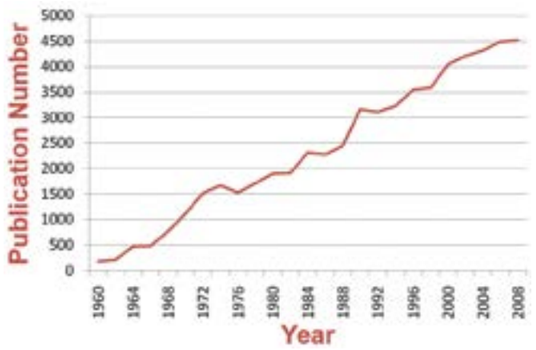


Figure 1. Annual publication rate of papers on virus/viruses AND cancer, as retrieved by PubMed

Viruses: From One Extreme to Another

At the turn of one century, 1900, there were many theories regarding the causes of malignancies. These included: 1) a transformation of cells of a tissue into cells of a different kind, 2) trauma accompanied by long-continued irritation, 3) change in control, by ovaries or testicles, of proliferation, 4) yeasts and lower fungi, and 5) parasites.[1-3] In this pre-gene era, transformation of cells was dismissed as an outdated concept.[1] While trauma and chronic inflammation were acknowledged as "powerful factors, and even adjuvants, in this disease", they seemed to lack the power to generate "true cancer cells".[1] The focus on reproductive organs foreshadowed the concept of hormones, introduced in 1902. The "inoculation into lower animals in various ways of portions of cancer growths of man", by producing tumors, demonstrated that transformation, trauma, or ovaries were not needed to produce cancerous growth. Clearly, something was in the tumor. Several scientists reported they were able to visualize microscopic "cancer bodies" of various shapes and sizes. However, infecting animals with various bacteria, fungi, or parasites could not produce true tumors.

Viruses were first identified in the 1890's as causative agents in various animal and plant diseases. The simplest way to screen for viruses involved filtering: if a cell-free filtrate from a tissue homogenate could cause a disease, then a virus was implicated. Homogenates from tumors were tested in many different ways, including filtration, and all of the evidence suggested that cellular material that could be propagated on certain broths under specific conditions was necessary to propagate a tumor from one animal to another. In 1911, Francis Peyton Rous demonstrated that a cell-free filtrate from a chicken sarcoma could be transferred to another bird to induce a tumor. These results were strongly questioned at the time, in part because many others had tried the same thing with other tumors and failed. In spite of the questions, Rous lived to receive, 55 years later, a Nobel Prize for his discovery that a virus can cause a tumor. This extended period between discovery and acknowledgment underscores the doubt, supported by abundant negative experimentation over many years, that viruses can be oncogenic.

Oncogene	Virus	Species
abl	Abelson leukemia	Mouse
akt	AKT8 virus	Mouse
cbl	Cas NS-1	Mouse
crk	CT10 sarcoma	Chicken
erbA	Avian erythroblastosis-ES4	Chicken
erbB	Avian erythroblastosis-ES4	Chicken
ets	Avian erythroblastosis-E26	Chicken
fes	Gardner-Arnstein feline sarcoma	Cat
fgr	Gardner-Rasheed feline sarcoma	Cat
fms	McDonough feline sarcoma	Cat
fos	FBJ murine osteogenic sarcoma	Mouse
fps	Fujinami sarcoma	Chicken
jun	Avian sarcoma-17	Chicken
kit	Hardy-Zuckerman feline sarcoma	Cat
maf	Avian sarcoma AS42	Chicken
mos	Moloney sarcoma	Mouse
mpl	Myeloproliferative leukemia	Mouse
myb	Avian myeloblastosis	Chicken
myc	Avian myelocytomatosis	Chicken
p3k	Avian sarcoma-16	Chicken
qin	Avian sarcoma-31	Chicken
raf	3611 murine sarcoma	Mouse
rasH	Harvey sarcoma	Rat
rasK	Kirsten sarcoma	Rat
rel	Reticuloendotheliosis	Turkey
ros	UR2 sarcoma	Chicken
sea	Avian erythroblastosis-S13	Chicken
sis	Simian sarcoma	Monkey
ski	Avian SK	Chicken
src	Rous sarcoma	Chicken
yes	Y73 sarcoma	Chicken

Table 1. Retroviral Oncogenes

A century later, in the new millenium, the picture is clearer: while viruses can cause cancer, few can do it by themselves. Put another way, most viruses do a nice job of infecting their hosts, but only a few of these infections go on to drive cancer. Something in those unlucky few hosts is needed in addition to the viral infection. For example, human papillomavirus (HPV) is a double-stranded DNA virus of the family Papovaviridae that includes over 100 'types', based on DNA homology. Several types infect the epithelium, particularly in the anogenital region. Many types of HPV cause no symptoms, while other types induce benign papillomatous lesions of skin and mucous membranes (anogenital warts, common warts, plantar warts, laryngeal papillomas). Only a few types of HPV, including types 16 and 18, produce papillomas that may, in rare cases, progress to cancers of the anogenital region. Nearly all cases of cervical cancer are due to HPV infection, although most infections with these types of HPV do not progress to cancer. Cofactors are required for cancer development.

More about Rous' Virus

Why is the Rous sarcoma virus (RSV) oncogenic? RSV is a retrovirus, which means that it replicates by making a DNA copy of its RNA genome by reverse transcription. Some retroviruses are able to infect cells and replicate without causing cell transformation, whereas other retroviruses are highly carcinogenic. What do oncogenic retroviruses have that others do not? In the case of RSV, it's an oncogene that was named src, as it causes sarcomas. The RSV oncogene was renamed v-src, denoting its viral origin, since mammals were found to have a similar gene, c-src (cellular-src). The protein product of v-src is pp60vsrc, a tyrosine kinase involved in signaling pathways that regulate cell movement, proliferation, and invasiveness. Oncogenes from other retroviruses encode many types of proteins that have important roles in pathways related to cell proliferation (Table 1).

Interestingly, the genome of RSV is essentially identical to that of the non-oncogenic avian leukosis virus, ALV, except that RSV contains v-src. It is now thought that retroviruses become oncogenic by incorporating a host cell's gene (the 'proto-oncogene') into the viral genome by a virus-host recombination event. In the virus, the host gene is regulated by viral promoter and enhancer elements. For this reason, oncogenes are expressed at high levels and may be transcribed in inappropriate cell types. Furthermore, the oncogene may encode a protein that differs structurally from the proto-oncogene product. For example, the viral protein may be truncated at either end, or have a portion of a different viral protein fused to it. Such deletions or insertions may result in the loss of regulatory domains that control protein activity. For example, the viral version of Raf is a fusion protein, with a second viral protein, Gag, fused where the host regulatory domain would normally be found. As a result, viral Raf is constitutively active, driving activation of kinases involved in proliferation, apoptosis and migration.

An *H. pylori* Story

Speaking of Nobel caliber work, two Australians, Robin Warren and Barry Marshall were awarded the Nobel Prize in Physiology or Medicine in 2005 for discovering the bacterium *Helicobacter pylori* and outlining its role in gastritis and peptic ulcer disease. Early in the 1980's, stress and lifestyle were considered the major causes of peptic ulcer disease. The dominant modes of treatment centered on reducing acid production using histamine H_2-receptor antagonists and, if necessary, surgery.[4] Marshall and Warren published a report in 1984 on 'unidentified curved bacilli' in the stomach of patients with ulceration,[5] and, within a decade, eradication of this new bacterium, *H. pylori*, became the focus of treatment around the world.

H. pylori is a spiral-shaped Gram-negative bacterium that colonizes the lower part of the stomach, at the antrum near the pylorus (Figure 3). The presence of *H. pylori* is always associated with inflammation of the underlying gastric mucosa with an infiltration of inflammatory cells. Chronic inflammation of the distal part of the stomach leads to increased acid production in the non-infected upper region of the stomach. *H. pylori* causes gastritis and peptic (gastric and duodenal) ulcers, but not gastroesophageal reflux disease. While over half the world's population is believed to be infected with this bacterium, infection is typically asymptomatic. On the other hand, the vast majority of peptic ulcers are caused by this pathogen.

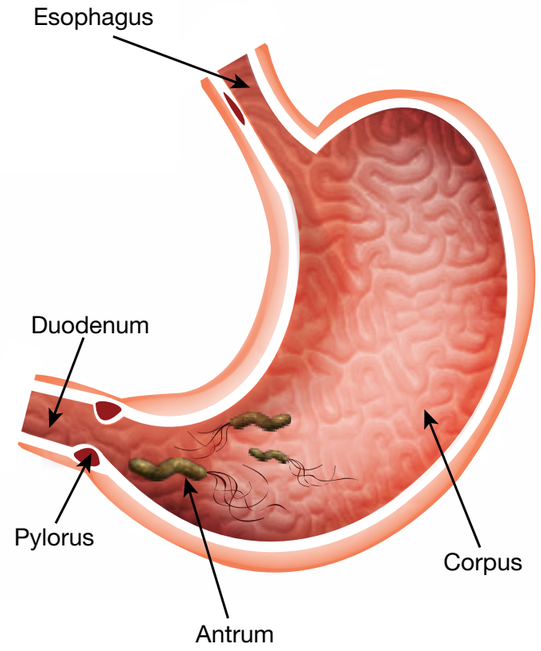


Figure 2. *H. pylori* typically reside in the antrum of the stomach, whereas the greatest acid secretion, ulceration, and tumor formation occur in the body, or corpus, of the stomach.

H. pylori also causes stomach cancer. In fact, it is the first bacterium to be classified as a definite carcinogen by the World Health Organization's International Agency for Research on Cancer.[6] While reports linking *H. pylori* and cancer emerged shortly after the bacterium's discovery, the mechanism of carcinogenesis remains elusive. Risk factors include virulence factors of the bacterium (*e.g.*, CagA, VacA), environmental factors (diet, smoking), and host factors (gene polymorphisms).[7,8] This brings us full circle to the 'hot topics' mentioned at the start of this article: genetics,[9] epigenetics,[10] molecular pathways,[11] and even stem cells[12] are fair game in current theories on how *H. pylori* infection leads to gastric cancer. In the end, these may just be the details that dress up the 'trauma accompanied by long-continued irritation' model put forth over 100 years ago.

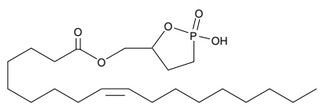
References

1. Beatson, G.T. *Br. Med. J.* **1(1990)**, 399-400 (1899).
2. Pease, H.D. *Public Health Pap Rep.* **1899(25)**, 607-614 (1899).
3. Nichols, E.H. *J. Boston Soc. Med. Sci.* **5(2)**, 34-58 (1900).
4. Grossman, M.I., Kurata, J.H., Rotter, J.I., *et al. Ann. Intern. Med.* **95(5)**, 609-627 (1981).
5. Marshall, B.J. and Warren, J.R. *Lancet* **1(8390)**, 1311-1315 (1984).
6. Amieva, M.R. and El-Omar, E.M. *Gastroenterology* **134(1)**, 306-323 (2008).
7. Wex, T., Bornschein, J., and Malfertheiner, P. *Minerva Gastroenterol. Dietol.* **55(4)**, 395-408 (2009).
8. González, C.A. and López-Carrillo, L. *Scand. J. Gastroenterol.* **45(1)**, 6-14 (2010).
9. Machado, A.M., Figueiredo, C., Seruca, R., *et al. Biochem. Biophys. Acta.* **1806(1)**, 58-65 (2010).
10. Ding, S.Z., Goldberg, J.B., and Hatakeyama, M. *Future Oncol.* **6(5)**, 851-862 (2010).
11. Oguma, K., Oshima, H., and Oshima, M. *Future Oncol.* **6(4)**, 515-526 (2010).
12. Saikawa, Y., Fukada, K., Takahashi, T., *et al. Gastric Cancer* **13(1)**, 11-24 (2010).

Oleoyl 3-carbacyclic Phosphatidic Acid 10010299

3-ccPA 18:1
MF: $C_{22}H_{41}O_5P$ **FW:** 416.5 **Purity:** ≥95%
A solution in chloroform **Stability:** ≥1 year at -20°C
Summary: A cyclic LPA analog that contains the 18:1 fatty acid, oleate, at the *sn*-1 position; at 25 µM, inhibits the transcellular migration of MM1 cells across mesothelial cell monolayers without affecting proliferation; at 0.1-1.0 µM, significantly inhibits autotaxin and antagonizes LPA_1 (IC_{50} = 836 nM) and LPA_3 (IC_{50} = 440 nM)

500 µg
1 mg
5 mg
10 mg



(2-hydroxy-2-oxido-1,2-oxaphospholan-5-yl)methyl ester-9Z-octadecenoic acid

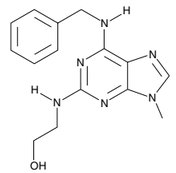
• Also Available: **Palmitoleoyl 3-carbacyclic Phosphatidic Acid** (10010298)
500 µg
1 mg
5 mg
10 mg

Palmitoyl 3-carbacyclic Phosphatidic Acid (10010293)
500 µg
1 mg
5 mg
10 mg

Olomoucine 10010240

[101622-51-9]
MF: $C_{15}H_{18}N_6O$ **FW:** 298.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An ATP-competitive CDK inhibitor; inhibits CDC2/cyclin B (IC_{50} = 7 µM), CDK2/cyclin A (IC_{50} = 7 µM), CDK2/cyclin E (IC_{50} = 7 µM, CDK/p35 kinase (IC_{50} = 3 µM), and ERK1/p44 MAPK (IC_{50} = 25 µM)

1 mg
5 mg
10 mg
25 mg



2-[[9-methyl-6-[(phenylmethyl)amino]-9H-purin-2-yl]amino]-ethanol

p38 MAPK Monoclonal Antibody (Clone 9F12) 10011301

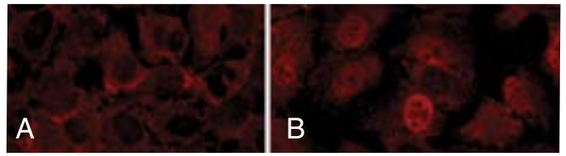
p38 MAPKα
Supplied as: IgG_1 **Stability:** ≥1 year at -20°C
Summary: Antigen: human full length p38 MAPK • Host: mouse, clone 9F12 • Cross Reactivity: (+) human, murine, and rat p38 MAPK • Application(s): FC, ICC, and WB • p38 MAPK is a member of the serine-threonine MAPK family that triggers many cellular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

1 ea

Phosphorylation/Translocation Assay Kit 10010374

Stability: ≥1 year at -20°C
Summary: p38 MAPK is activated by phosphorylation at Thr^{180} and Tyr^{182} in response to both inflammatory cytokines and stress. The subcellular location of p38 following stimulation is not well understood. Cayman's p38 Cell-Based 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, for treatment of cells, is included as a positive control.

1 ea



Inhibition of network formation by JNJ-10198409. *Panel A:* CAPE cells suspended in culture medium containing 0.064 µM PMA or *Panel B:* 0.064 µM PMA + 0.3 µM JNJ-10198409 were seeded at a density of 6 x 10^3 cells/well in a 96-well plate and grown in 37°C incubator for four days. On the fifth day, cells were stained with Calcein AM and the organization was examined under an inverted fluorescence microscope.

p38 MAPK (Phospho-Thr180/Tyr182) Polyclonal Antibody 10009177

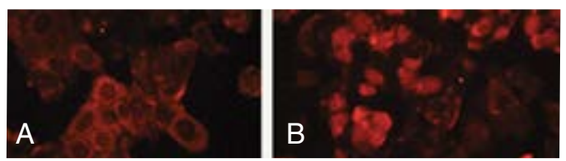
Supplied as: Affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: phosphopeptide corresponding to amino acid residues surrounding phospho-Thr^{180} and phospho-Tyr^{182} of rat p38 MAPK • Host: rabbit • Cross Reactivity: (+) human p38 • Application(s): WB • p38 MAPK is activated by 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

p38 MAPK (Phospho-Thr180/Tyr182) Cell-Based 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 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 the monoclonal antibody. Translocation of p53 from cytoplasm to nuclei upon stimulation by (-)-Nutlin-3 is evident.

p53 Monoclonal Antibody (Clone BP53-12) 10004806

Supplied as: 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 • Cross Reactivity: (+) human p53 • Application(s): FC, ICC, IHC (paraffin-embedded sections), and WB; this antibody does not work with frozen sections • Isotype: IgG_{2a} • Clone designation: BP53-12

1 ea

p53 (Phospho-Ser392) Polyclonal Antibody 10004807

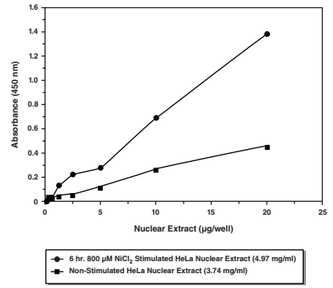
Supplied as: Affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: amino acids around phospho-Ser^{392} • Host: rabbit • Application(s): WB • Nearly 50% of human tumors have mutated or non-functional p53. p53 amino acid residues can be modified by phosphorylation and acetylation. *In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

1 ea

p53 Transcription Factor Assay Kit 600020

Stability: ≥1 year at -80°C
Summary: 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 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 provides a sensitive colorimetric readout at 450 nm.

96 wells



• Also Available: **p53 Designer Transcription Factor Assay Kit** (600030)
96 wells

p53 Total and p53 (Phospho-Ser392) Dual Staining Assay Kit (600060) 96 wells

p66α Polyclonal Antibody 13785

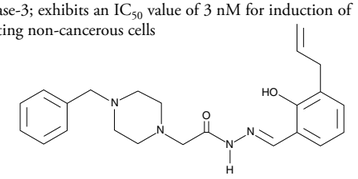
GATA Zinc Finger Domain-Containing Protein 2A, Transcriptional Repressor p66α
Supplied as: IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: synthetic peptide corresponding to mouse p66α amino acids 575-585 • Host: rabbit • Cross Reactivity: (+) human, murine, and rat p66α • Application(s): WB • p66, a zinc finger-containing protein, is one of the components of the MeCP1 complex. p66 and p68, the two components of MeCP1, are different forms of the same zinc finger-containing protein and are conserved from *C. elegans* to humans. Homologs of p66 from different organisms revealed two highly conserved regions, CR1 and CR2. While CR1 is involved in the association of p66 with other MeCP1 components, CR2 plays an important role in targeting p66 and MBD3 to specific loci.

1 ea

PAC-1 10009317

[315183-21-2] Procaspase-Activating Compound 1
MF: $C_{23}H_{28}N_4O_2$ **FW:** 392.5 **Chemical 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

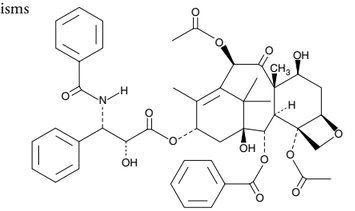


4-(phenylmethyl)-[[2-hydroxy-3-(2-propenyl)phenyl]methylene]hydrazide, 1-piperazineacetic acid

Paclitaxel 10461

[33069-62-4] NSC 125973, Taxol®
MF: $C_{47}H_{51}NO_{14}$ **FW:** 853.9 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent disruptor of microtubules used as a chemotherapeutic compound; inhibits growth of cervical (HeLa), lung (A549), breast (MCF-7), colon (HT-29), ovarian (OVG-1), and pancreatic (PC-Sh) carcinomas with IC_{50} values ranging from 2.5-7.5 nM; induces mitotic arrest and initiates apoptosis of cancer cells through multiple mechanisms

5 mg
25 mg
50 mg
100 mg



β-(benzoylamino)-a-hydroxy-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2aR,3,4S,4aS,5,6R, 9S,10,11S,12S,12aR,12bS-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, benzenepropanoic acid

PARP (Cleaved) Monoclonal Antibody 13557

Supplied as: Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: synthetic peptide containing amino acids near the 214/215 cleavage site of human PARP • Isotype: $IgG_{2bκ}$ • Host: mouse • Cross Reactivity: (+) human PARP • Application(s): FC (intracellular) and WB • PARP is a 116 kDa nuclear chromatin-associated enzyme that is cleaved during apoptosis by caspase-3 into a 24 kDa fragment containing the DNA binding domain and an 89 kDa fragment containing the catalytic and automodification domains. The 24 kDa fragment irreversibly binds to DNA and may contribute to the irreversibility of apoptosis by blocking the access of DNA repair enzymes to DNA strand breaks.

1 ea

pCAF Histone Acetyltransferase (human recombinant) 10009115

p300/(CREB binding protein) Associated Factor, HAT
Purity: ≥95%
Supplied as: A solution in 50 mM sodium phosphate, pH 7.2, containing 100 mM sodium chloride, 1 mM EDTA, and 20% glycerol
Stability: ≥6 months at -80°C
Summary: Source: recombinant GST-tagged protein purified from *E. coli* • M_r: ~40 kDa • pCAF belongs to the GCN5/pCAF family of nuclear HATs. Cayman's pCAF preparation contains 165 amino acids from the HAT activity domain of human pCAF fused to GST at the N-terminus. Enzyme activity was determined using a fluorescent HAT assay and is comparable to that found in the literature.

25 µg
50 µg
100 µg

PCNA Monoclonal Antibody (Clone IPO-38) 10004805

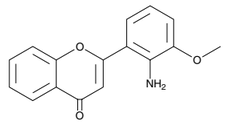
Proliferating Cell Nuclear Antigen
Supplied as: Purified IgM **Stability:** ≥1 year at 4°C
Summary: Host: mouse, clone IPO-38 • Cross Reactivity: (+) multiple species (species- and tissue-unspecific) • Application(s): FC, ICC, IHC (frozen and paraffin-embedded sections), and WB • PCNA becomes detectable in the G_1 phase of the cell cycle and reaches a maximum level of expression during mitosis. PCNA is highly conserved across species and is a critical part of the DNA polymerase holoenzyme. The level of PCNA expression depends on the proliferative potential of the cell examined.

1 ea

PD 98059 10006726

[167869-21-8]
MF: $C_{16}H_{13}NO_3$ **FW:** 267.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A selective, noncompetitive inhibitor of the MAPK pathway; prevents the activation of MAPKK1 by Raf or MEK kinase with an IC_{50} value of 2-7 µM

1 mg
5 mg
10 mg
50 mg

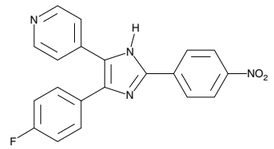


2-(2-amino-3-methaxyphenyl)-4H-1-benzopyran-4-one

PD 169316 10006727

[152121-53-4]
MF: $C_{20}H_{13}FN_4O_2$ **FW:** 360.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A selective inhibitor of p38 MAPK (IC_{50} = 89 nM)

1 mg
5 mg
10 mg
25 mg

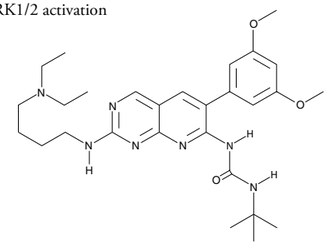


4-[5-(4-fluorophenyl)-2-(4-nitrophenyl)-1H-imidazol-4-yl]-pyridine

PD 173074 13032

[219580-11-7]
MF: $C_{28}H_{41}N_7O_3$ **FW:** 523.7 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent, selective inhibitor of FGFR tyrosine kinase activity, blocking autophosphorylation of FGFR1 (IC_{50} = 21.5 nM); impairs angiogenesis, as well as self-renewal of stem cells *via* ERK1/2 activation

500 µg
1 mg
5 mg
10 mg

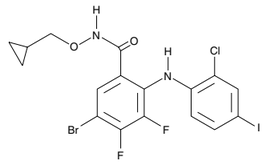


N-[2-[[4-(diethylamino)butyl]amino]-6-(3,5-dimethoxyphenyl)pyrido[2,3-d] pyrimidin-7-yl]-N'-(1,1-dimethylethyl)-urea

PD 184161 10012431

[212631-67-9]
MF: $C_{17}H_{13}BrClF_2IN_2O_2$ **FW:** 557.6 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent and selective inhibitor of MEK1/2 (IC_{50} = 10-100 nM)

1 mg
5 mg
10 mg
25 mg

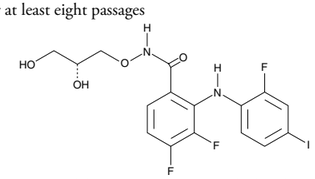


5-bromo-2-[(2-chloro-4-iodophenyl)amino]-N-(cyclopropylmethoxy)-3,4-difluoro-benzamide

PD 0325901 13034

[391210-10-9]
MF: $C_{16}H_{14}F_3IN_2O_4$ **FW:** 482.2 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent MEK inhibitor that suppresses phosphorylation of ERK in murine colon 26 tumors with an IC_{50} value of 0.33 nM; suppression of ERK activation with 1 µM PD 0325901 combined with 3 µM CHIR99021 (a glycogen synthase kinase-3 inhibitor) prevents cell differentiation and sustains self renewal of murine embryonic stem cells for at least eight passages

500 µg
1 mg
5 mg
10 mg



N-[(2R)-2,3-dihydroxypropoxy]-3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]-benzamide

PH Domain Leucine-rich Repeat Protein Phosphatase Polyclonal Antibody 10007191

KIAA0606 Protein, PHLPP, PLEKHE1 Protein, SCOP, Suprachiasmatic Nucleus Circadian Oscillatory Protein
Supplied as: Peptide affinity-purified IgG **Stability:** ≥1 year at 4°C
Summary: Antigen: human PHLPP amino acids 1192-1205 • Host: rabbit • Cross Reactivity: (+) human, murine, and rat PHLPP • Application(s): ICC, IHC (paraffin-embedded sections), and WB • PHLPP dephosphorylates the hydrophobic motif of Akt and thus reduces Akt activity, resulting in an increase in the number of apoptotic cells. PHLPP levels are markedly reduced in several colon cancer and glioblastoma cell lines that have elevated Akt phosphorylation.

500 µl

• Also Available: **PH Domain Leucine-rich Repeat Protein Phosphatase Blocking Peptide** (10007192) 1 ea

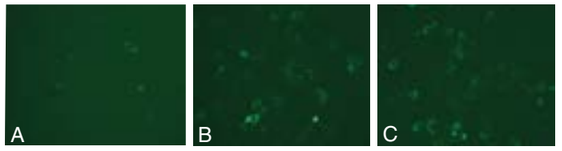
PI3K/Akt Pathway Inhibitors

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
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
70920	LY294002	PI3K	IC_{50} = 1.4 µM
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
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	p110α	IC_{50} = 5.8 nM
13067	SB 203580	PDK-1	IC_{50} = 3-5 µM
10007349	TGX-221	PI3K p110β	IC_{50} = 50 nM in platelets
10010237	Triciribine	Akt	IC_{50} = ~ 5-10 µM in Akt-overexpressing human cancer cell lines
10010591	Wortmannin	PI3K	IC_{50} = 1-10 nM

Phagocytosis Assay Kit (IgG FITC) 500290

Stability: ≥6 months at 4°C
Summary: Cayman's Phagocytosis Assay (IgG FITC) employs latex beads coated with fluorescently-labeled rabbit-IgG as a probe for the identification of factors regulating the phagocytic process *in vitro*. The engulfed fluorescent-beads can be detected by fluoresence microscopy or flow cytometry.

1 ea

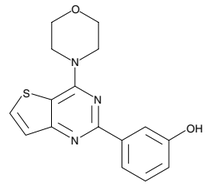


PMA induces the differentiation of THP-1 cells into phagocytic cells. THP-1 cells were treated with either vehicle (*Panel A*), 0.16 µM PMA (*Panel B*), or 1.6 µM PMA (*Panel C*) and at the same time loaded with Latex Beads-Rabbit IgG-FITC Complex. PMA treatment at a dose as low as 0.16 µM caused THP-1 cells to differentiate and become phagocytic, as evidenced by a significant increase in cells engulfing the Latex Beads-Rabbit IgG-FITC complex.

PI3-Kinase α Inhibitor 2 10010177

[371943-05-4] PI3Kα Inhibitor 2, Phosphatidylinositol 3-Kinase α Inhibitor 2
MF: $C_{16}H_{15}N_3O_2S$ **FW:** 313.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A selective inhibitor of PI3Kα with IC_{50} values of 2, 16, 660, and 220 nM for the α, β, γ, and C2β isoforms, respectively

500 µg
1 mg
5 mg
10 mg

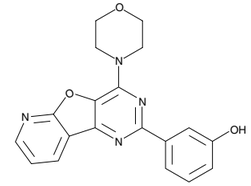


3-[4-(4-morpholinyl)thieno[3,2-d]pyrimidin-2-yl]-phenol

PI-103 10009209

[371935-74-9]
MF: $C_{19}H_{16}N_4O_3$ **FW:** 348.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent, cell-permeable, ATP-competitive inhibitor of PI3K family members (IC_{50} = 2, 8, 20, and 26 nM for DNA-PK, p110α, mTORC1, and PI3-KC2β, respectively)

1 mg
5 mg
10 mg
25 mg

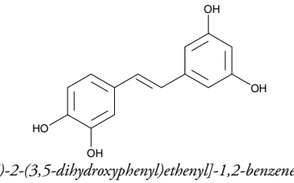


3-[4-(4-morpholinyl)pyrido[3',2':4,5]furo[3,2-d]pyrimidin-2-yl]-phenol

Piceatannol 10009366

[10083-24-6] Astringenin, trans-3,3',4,5'-Tetrahydroxystilbene
MF: $C_{14}H_{12}O_4$ **FW:** 244.2 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A resveratrol analog that exhibits potent anticancer properties; induces apoptosis in BJAB Burkitt-like lymphoma cells with an ED_{50} value of 25 µM

5 mg
10 mg
25 mg
50 mg

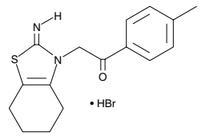


4-[(1E)-2-(3,5-dihydroxyphenyl)ethenyl]-1,2-benzenediol

Pifithrin-α 13326

[63208-82-2]
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

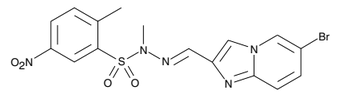


1-(4-methylphenyl)-2-(4,5,6,7-tetrahydro-2-imino-3(2H)-benzothiazolyl)-ethanone, monohydrobromide

PIK-75 10009210

[372196-67-3]
MF: $C_{16}H_{14}BrN_5O_4S$ **FW:** 452.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A selective inhibitor of p110α with an IC_{50} value of 5.8 nM; inhibits p110γ and p110β with IC_{50} values of 0.076 µM and 1.3 µM, respectively

1 mg
5 mg
10 mg
25 mg

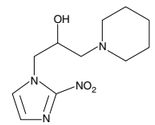


2-methyl-5-nitro-2-[(6-bromoimidazo[1,2-a]pyridin-3-yl)methylene]-1-methylhydrazide-benzenesulfonic acid

Pimonidazole 89130

[70132-50-2] NSC 380540, Ro 03-8799
MF: $C_{11}H_{18}N_4O_3$ **FW:** 254.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A small molecule radiosensitizer that has proven to be an effective and nontoxic immunochemical hypoxia marker for human squamous cell carcinomas of the cervix, head, and neck

5 mg
10 mg
50 mg
100 mg



α-[(2-nitro-1H-imidazol-1-yl)methyl]-1-piperidineethanol

PINK1 Polyclonal Antibody 10006283

BRPK, PARK6, PTEN Induced Putative Kinase 1
Supplied as: Peptide affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human PINK1 amino acids 484-504 • Host: rabbit • Cross Reactivity: (+) human, murine, and rat PINK1 protein • 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.

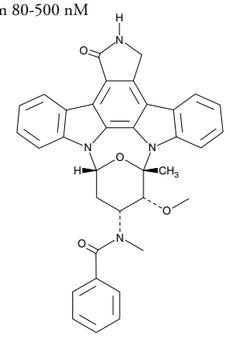
500 µl

• Also Available: **PINK1 Blocking Peptide** (10006284) 1 ea

PKC 412 10459

[120685-11-2] N-Benzoylstaurosporine, CGP 41231, CGP 41251, Midostaurin
MF: $C_{35}H_{30}N_4O_4$ **FW:** 570.6 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A cell-permeable, reversible inhibitor of several kinases, including PKCα, PKCβ, PKCγ, Syk, Flk-1, Akt, PKA, c-Kit, C-Fgr, c-Src, FLT3, PDFRβ, VEGFR1, and VEGF2, with IC_{50} values ranging from 80-500 nM

1 mg
5 mg
10 mg
50 mg

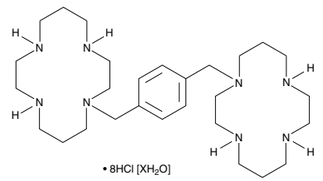


N-[(9S,10R,11R,13R)-2,3,10,11,12,13-hexahydro-10-methoxy-9-methyl-1-oxo-9,13-epoxy-1H,9H-diindolo[1,2,3-gh:3',2',1'-lm]pyrrolo[3,4-j][1,7]benzodiazonin-11-yl]-N-methyl-benzamide

Plerixafor (hydrochloride hydrate) 10011332

[155148-31-5] AMD 3100, JM 3100, Mobozil™, SID 791
MF: $C_{28}H_{54}N_8$ • 8HCl • $[XH_2O]$ **FW:** 794.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An irreversible antagonist of CXCR4 which suppresses infection by CXCR4-tropic HIV with an IC_{50} value of 1-10 ng/ml; mobilizes hematopoietic stem cells and progenitor cells as well as mature T-cells; regulates growth and metastasis of cancer cells

1 mg
5 mg
10 mg
50 mg



1,4-bis((1,4,8,11-tetraazacyclotetradecan-1-yl)methyl)benzene, octahydrochloride

PMS2 Monoclonal Antibody (Clone 163C1251) 13786

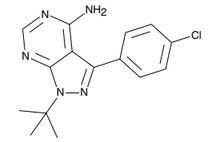
DNA Mismatch Repair Protein PMS2, Mismatch Repair Endonucleas PMS2, PMS1 Protein Homologue 2
Supplied as: Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: synthetic peptide from human PMS2 amino acids 623-639 • Host: mouse, clone 163C1251 • Isotype: Mouse IgG_1 • Cross Reactivity: (+) murine and human PMS2 • Application(s): WB • PMS2 is a DNA mismatch repair protein. Defects in PMS2 are a cause of hereditary non-polyposis cancer (HNPCC). Human PMS2 is a protein of 862 amino acids.

1 ea

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: p56lck (IC_{50} = 4 nM), p59fynT (IC_{50} = 5 nM), and Hck (IC_{50} = 5 nM)

1 mg
5 mg
10 mg
25 mg

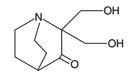


3-(4-chlorophenyl)-1-(1,1-dimethylethyl)-1H-pyrazolo[3,4-d]pyrimidin-4-amine

PRIMA-1 63520

[5608-24-2]
MF: $C_9H_{15}NO_3$ **FW:** 185.2 **Purity:** ≥95%
A crystalline solid **Stability:** ≥1 year at -20°C
Summary: A unique anti-oncogenic substance that acts as a re-activator of the apoptotic function of mutant p53

1 mg
5 mg
10 mg
50 mg



2,2-bis(hydroxymethyl)-3-quinuclidinone

PRMT1 (human recombinant) 10350

Purity: ≥80%
Supplied as: A solution in 50 mM Tris-HCl, pH 8.0, containing 150 mM sodium chloride and 20% glycerol **Stability:** ≥6 months at -80°C
Summary: Source: human recombinant N-terminal GST-tagged protein expressed in *E. coli* • M_r: 69.2 kDa • PRMT1 is a class I arginine methyltransferase that methylates arginine residues at a number of glycine and arginine rich regions (GAR motifs) including histone H4 at arginine 3.

25 µg
50 µg
100 µg

PRMT4 Polyclonal Antibody 13552

CARM1
Supplied as: Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: synthetic peptide corresponding to human PRMT4 amino acid sequences 45-69 and 595-608 • Host: rabbit • Cross Reactivity: (+) human PRMT4 • Application(s): WB • PRMT4, also known as CARM1, belongs to a family of proteins that catalyzes the methylation of arginine residues.

1 ea

PRMT5 Polyclonal Antibody 13559

JBP1, Skb1HS
Supplied as: Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: synthetic peptide from human PRMT5 • Host: rabbit • Cross Reactivity: (+) human PRMT5 • Application(s): WB • PRMT5, also known as JBP1 and human homolog of Skb1 of fission yeast (Skb1HS) can catalyze the formation of ω-N^G-monomethylarginine and symmetric ω-N^G,$N^{G'}$-dimethylarginine in a variety of proteins. Recombinant PRMT5 can mono- and dimethylate histone 2A and myelin basic protein.

1 ea

PRMT6 Polyclonal Antibody 13558

Supplied as: Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: synthetic peptide from human PRMT6 amino acids 23-43 • Host: rabbit • Cross Reactivity: (+) human and murine PRMT6 • Application(s): WB • PRMT6 is a protein with an approximate molecular weight of 42 kDa consisting of a catalytic core sequence common to other PRMT enzymes. PRMT6 demonstrates type 1 PRMT activity, capable of forming both N^G-monomethylarginine and asymmetric N^G,N^G-dimethylarginine derivatives on recombinant glycine- and arginine-rich substrates.

1 ea

PRMT7 Polyclonal Antibody 13551

Supplied as: Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: synthetic peptide from human PRMT7 amino acid sequence 346-360 • Host: rabbit • Cross Reactivity: (+) human and murine PRMT7 • Application(s): WB • PRMT7 can catalyze the formation of ω-N^G-monomethylarginine in peptides.

1 ea

Programmed Cell Death Protein 4 (C-Term) Polyclonal Antibody 10250

Neoplastic Transformation Inhibitor, PDCD4
Supplied as: Peptide-affinity purified IgG polyclonal **Stability:** ≥1 year at -20°C
Summary: Antigen: human PDCD4 C-terminal amino acids 458-468 • Host: rabbit • Cross Reactivity: (+) human, murine, and rat PDCD4 • Application(s): WB • PDCD4 levels are elevated during apoptosis and absent in many cancer samples. Loss of PDCD4 expression is an important event in cancer cell progression whereas the restoration of PDCD4 protein can lower metalloproteinase activity and possible metastasis.

500 µl

• Also Available: **Programmed Cell Death Protein 4 (C-Term) Blocking Peptide** (13365) 200 µg

15-hydroxy Prostaglandin Dehydrogenase (human recombinant) 10007950

15-hydroxy PGDH
Purity: ≥95% by SDS-PAGE
Supplied as: A solution in 50 mM Tris-HCl, pH 7.5, containing 1 mM EDTA, 1 mM DTT, and 30% glycerol **Stability:** ≥6 months at -80°C
Summary: Source: human recombinant N-terminal GST-tagged protein expressed in *E. coli* • M_r: 55 kDa • NAD^+-dependent 15-PGDH catalyzes the oxidation of PGs to 15-keto metabolites that have greatly reduced biological activity. Three different studies have shown an inverse correlation between 15-PGDH expression and cell proliferation in colon, breast, and thyroid cells.

25 µg
50 µg
100 µg

15-hydroxy Prostaglandin Dehydrogenase Polyclonal Antibody 160615

15-hydroxy PGDH, PG15DH
Supplied as: Peptide affinity-purified IgG **Stability:** ≥2 years at -20°C
Summary: Antigen: human NAD^+-dependent 15-hydroxy PGDH amino acids 92-105 • Host: rabbit • Cross Reactivity: (+) human, bovine, guinea pig, and baboon 15-hydroxy PGDH • Application(s): WB • NAD^+-dependent 15-hydroxy PGDH catalyzes the oxidation of PGs to 15-keto metabolites, which have greatly reduced biological activity. Three different studies have shown an inverse correlation between 15-PGDH expression and cell proliferation in colon, breast, and thyroid cells.

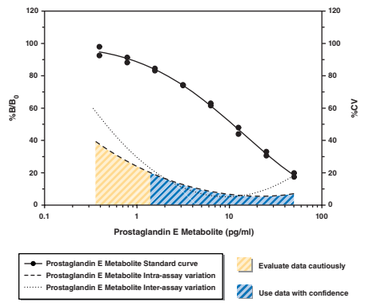
500 µl

• Also Available: **15-hydroxy Prostaglandin Dehydrogenase Blocking Peptide** (360615) 200 µg
15-hydroxy Prostaglandin Dehydrogenase Western Ready Control (10009742) 1 ea

Prostaglandin E Metabolite EIA Kit 514531

PGEM
Stability: ≥1 year at -20°C
Sensitivity: 50% B/B_0: 11 pg/ml • 80% B/B_0: 2 pg/ml
Summary: Because of the rapid metabolism of PGE_2, the determination of *in vivo* PGE_2 biosynthesis is often best accomplished by the measurement of PGE_2 metabolites. Cayman's PGEM assay converts all 13,14-dihydro-15-keto PGE_2 and 13,14-dihydro-15-keto PGA_2 into a single stable derivative, which is easily measurable by EIA. This assay is therefore the method of choice if the samples in question have undergone extensive metabolism prior to collection.

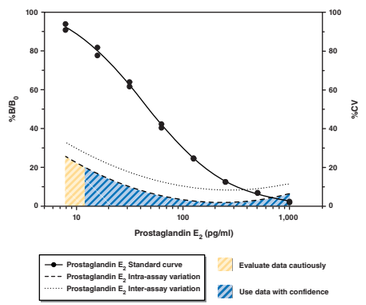
96 strip/solid wells
480 strip/solid wells



Prostaglandin E_2 EIA Kit - Monoclonal 514010

Stability: ≥1 year at -20°C
Sensitivity: 50% B/B_0: 50 pg/ml • 80% B/B_0: 15 pg/ml
Summary: Cayman's PGE_2 EIA is a sensitive competitive assay that uses a high-affinity PGE_2 monoclonal antibody for quantification of PGE_2 in plasma, urine, and culture media samples.

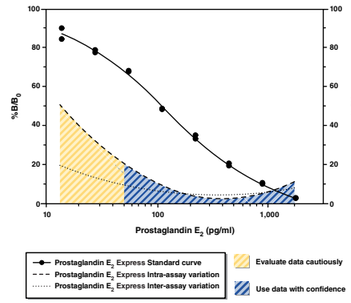
96 strip/solid wells
480 strip/solid wells



Prostaglandin E_2 Express EIA Kit 500141

Stability: ≥1 year at -20°C
Sensitivity: 50% B/B_0: 125 pg/ml • 80% B/B_0: 36 pg/ml
Summary: Cayman's PGE_2 Express EIA permits the rapid measurement of PGE_2 from biological samples, requiring only one hour incubation and development times for each step.

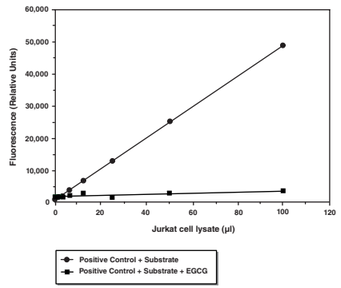
96 strip/solid wells
480 strip/solid wells



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. Proteasome inhibitors exhibit anti-inflammatory and antiproliferative effects. 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.

1 ea



Protein Arginine Deiminase 4 (human recombinant) 10500

PAD4
Purity: ≥95%
Supplied as: A solution in 50 mM sodium phosphate, pH 7.2, containing 100 mM sodium chloride, 1 mM EDTA, and 20% glycerol **Stability:** ≥9 months at -80°C
Summary: Source: Recombinant N-terminal His-tagged protein expressed in *E. coli* • M_r: 75.8 kDa • PAD4 is a homodimer that functions as a transcriptional coregulator to catalyze the conversion of specific arginine residues to citrulline in a calcium-dependent manner. PAD4 substrates include histones H2A, H3, and H4, whose post-translational modifications play a large role in gene regulation.

50 µg
100 µg
250 µg

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

PP2A Cα, PP2A L309, PP2A Δ^{309}
Purity: ≥90%
Supplied as: A solution in 20 mM Tris-HCl, pH 7.5, containing 100 mM sodium chloride, 1 mM EDTA, 1 mM DTT, 5 mM magnesium chloride, and 25% glycerol
Stability: ≥6 months at -80°C
Summary: Source: human recombinant PP2A catalytic subunit expressed in insect cells with an N-terminal octahistidine-tag followed by a streptactin-tag. The C-terminal leucine 309 was deleted. • M_r: 38.6 kDa • 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

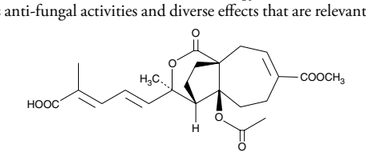
PTP1B
Purity: ≥95%
Supplied as: A solution in 100 mM Tris, pH 7.2, containing 100 mM sodium chloride, 1 mM EDTA, and 25% glycerol **Stability:** ≥6 months at -80°C
Summary: Source: human recombinant protein purified from *E. coli* • M_r: 37.3 kDa • PTPs remove phosphate from tyrosine residues of cellular 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

Pseudolaric Acid B 13527

[82508-31-4] PAB
MF: $C_{23}H_{28}O_8$ **FW:** 432.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A diterpene acid isolated from the bark of *P. kaempferi*, a traditional Chinese medicinal plant; has anti-fungal activities and diverse effects that are relevant to cancer therapy

500 µg
1 mg
5 mg
10 mg



4a-(acetyloxy)-3-[(1E,3E)-4-carboxy-1,3-pentadien-1-yl]-3R,4S,4aS,5,6,9-hexahydro-3-methyl-1-oxo-7-methyl ester;1H-4,9aR-ethanocyclohepta[c]pyran-7-carboxylic acid

PTEN (human recombinant) 10009746

MMAC1, Phosphatase and Tensin Homolog on Chromosome 10, Phosphatidylinositol 3-phosphatase, TEP1
Supplied as: A solution in 50 mM sodium phosphate, pH 7.2, containing 100 mM sodium chloride and 20% glycerol **Stability:** ≥6 months at -80°C
Summary: Source: human recombinant N-terminal His-tagged protein purified from *Sf*21 cells • M_r: 50.8 kDa • 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

PTEN Polyclonal Antibody 10005059

MMAC1, Phosphatase and Tensin Homolog on Chromosome 10, Phosphoinositide 3-phosphatase, TEP1
Supplied as: Peptide affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human PTEN amino acids 254-270 • Host: rabbit • Cross Reactivity: (+) human, murine, chimpanzee, canine, and rat PTEN • 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.

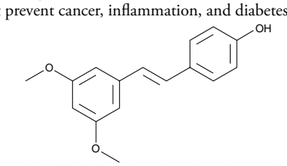
500 µl

• Also Available: **PTEN Blocking Peptide** (10007073) 1 ea
PTEN Western Ready Control (1009747) 1 ea

Pterostilbene 13000

[537-42-8] trans-3,5-Dimethoxy-4'-Hydroxystibene, 3',5'-Dimethoxy-4-Stilbenol
MF: $C_{16}H_{16}O_3$ **FW:** 256.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A naturally-occurring dimethyl ether analog of resveratrol; acts as a powerful antioxidant, suppresses the synthesis of PGE_2 from LPS-stimulated human peripheral blood mononuclear cells (IC_{50} = 1.0 µM), and inhibits cell proliferation (IC_{50} ~60 µM); evokes effects that prevent cancer, inflammation, and diabetes

50 mg
100 mg
250 mg
500 mg

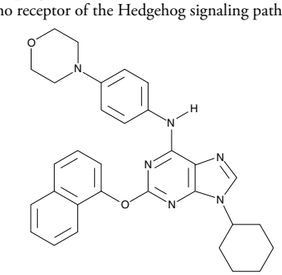


4-[(1E)-2-(3,5-dimethoxyphenyl)ethenyl)-phenol

Purmorphamine 10009634

[483367-10-8]
MF: $C_{31}H_{32}N_6O_2$ **FW:** 520.6 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A 2,6,9-trisubstituted purine that promotes the differentiation of both human and murine mesenchymal progenitor cells into osteoblasts; binds to and activates the 7-transmembrane Smo receptor of the Hedgehog signaling pathway

1 mg
5 mg
10 mg
25 mg



9-cyclohexyl-N-[4-(morpholinyl)phenyl]-2-(1-naphthalenyloxy)-9H-purin-6-amine

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

Supplied as: 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, murine, 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}.

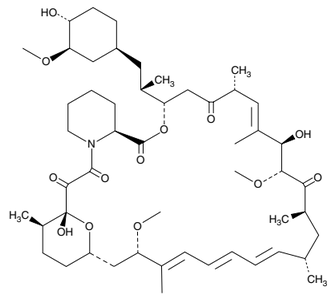
1 ea

• Also Available: **Raf-1 (Phospho-Ser^{642}) Polyclonal Antibody** (10009505) 1 ea

Rapamycin 13346

[53123-88-9] Sirolimus
MF: $C_{51}H_{79}NO_{13}$ **FW:** 914.2 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An immunosuppressant used to prevent transplant rejection; potent inhibitor of IL-2 activation of lymphocytes (IC_{50} = 5 pM); specifically interacts with FKBP12 to form a complex which inhibits mTORC1

1 mg
5 mg
10 mg
25 mg

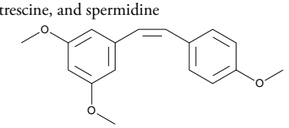


(7E,15E,17E,19E)-9,10,12,13,14,21,22,23,24,25,26,27,32,33,34aS-hexadecahydro-9R,27-dihydroxy-3S-[(1R)-2-[(1S,3R,4R)-4-hydroxy-3-methoxycyclohexyl]-1-methylethyl]-10R,21S-dimethoxy-6R,8,12R,14S,20,26R-hexamethyl-23S,27R-epoxy-3H-pyrido[2,1-c][1,4]oxaazacyclohentriacontine-1,5,11,28,29(4H,6H,31H)-pentone

cis-trismethoxy Resveratrol 13199

[94608-23-8] cis-Trimethoxy Stilbene
MF: $C_{17}H_{18}O_3$ **FW:** 270.3 **Purity:** ≥98%
A solution in ethanol **Stability:** ≥6 months at -20°C
Summary: A potent anti-mitotic drug that is 100-fold more active than resveratrol at inhibiting the growth of human colon cancer Caco-2 cells; inhibits tubulin polymerization in a dose-dependent manner (IC_{50} = 4 µM) and enzymes involved in the synthesis of the polyamines, putrescine, and spermidine

10 mg
50 mg
100 mg
500 mg

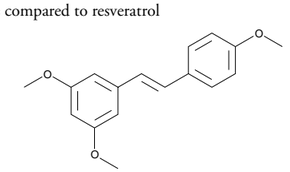


1,3-dimethoxy-5-[(1Z)-2-(4-methoxyphenyl)ethenyl]-benzene

trans-trismethoxy Resveratrol 10188

[22255-22-7] (E)-5-[2-(4-Hydroxyphenyl)ethenyl]-1,3-benzene diol
MF: $C_{17}H_{18}O_3$ **FW:** 270.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An analog of resveratrol in which the three phenolic hydroxyl groups of resveratrol are converted to methyl ethers; exhibits enhanced inhibition of cell growth and pro-apoptotic activities compared to resveratrol

50 mg
100 mg
250 mg
500 mg



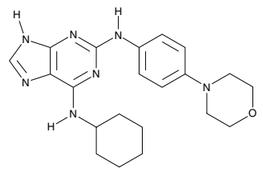
1,3-dimethoxy-5-[(1E)-2-(4-methoxyphenyl)ethenyl]-benzene

• Also Available: ***trans*-trismethoxy Resveratrol-d_4** (13129) 100 µg, 250 µg, 500 µg, 1 mg

Reversine 10004412

[656820-32-5]
MF: $C_{21}H_{27}N_7O$ **FW:** 393.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A 2,6-disubstituted purine derivative that causes dedifferentiation of cultured myoblasts into confluent stem cell progenitors

1 mg
5 mg
10 mg
25 mg

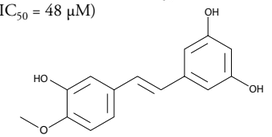


N6-cyclohexyl-N2-[4-(4-morpholinyl)phenyl]-1H-purine-2,6-diamine

Rhapontigenin 13293

[500-65-2]
MF: $C_{15}H_{14}O_4$ **FW:** 258.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A natural analog of resveratrol with antioxidant and anti-cancer activity; a mechanism-based, selective inactivator of CYP450 1A1 (IC_{50} = 400 nM); inhibits the proliferation of cancer cell lines (IC_{50} = 48 µM)

1 mg
5 mg
10 mg
25 mg



5-[(1E)-2-(3-hydroxy-4-methoxyphenyl)ethenyl]-1,3-benzenediol

RICK Polyclonal Antibody 160785

CARDIAK, CCk, RIP2, Ripk2
Supplied as: Affinity-purified IgG **Stability:** ≥1 year at 4°C
Summary: Antigen: human RICK amino acids 11-30 • Host: rabbit • Cross Reactivity: (+) human, murine, and rat RICK • 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.

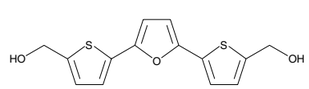
500 µl

• Also Available: **RICK Blocking Peptide** (301785) 200 µg

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

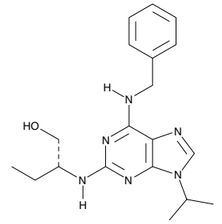


5,5'-(2,5-furandiyl)bis-2-thiophenemethanol

(R)-Roscovitine 10009569

[186692-46-6] Seliciclib
MF: $C_{19}H_{26}N_6O$ **FW:** 354.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent inhibitor of CDK2/cyclin E with an IC_{50} value of 0.1 µM; also inhibits CDK7/cyclin H, CDK5/p35, and cell division cycle (cdc)/cyclin B with IC_{50} values of 0.49, 0.16, and 0.65 µM

500 µg
1 mg
5 mg
10 mg



2-[[9-(1-methylethyl)-6-[(phenylmethyl)amino]-9H-purin-2-yl]amino]-1-butanol

$S1P_1$ Polyclonal Antibody 10005228

EDG-1, S1PR1, Sphingosine-1-Phosphate Receptor 1
Supplied as: Peptide affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human $S1P_1$ amino acids 241-253 • Host: rabbit • Cross Reactivity: (+) human, murine, porcine, and rat $S1P_1$ • Application(s): ICC, IHC (paraffin-embedded sections), and WB • S1P exerts its activity by binding to five distinct GPCRs, $S1P_1$ primarily mediates S1P-induced cell proliferation, survival, migration, cytoskeletal organization, and morphogenesis. Expression of $S1P_1$ is abundant in embryological vasculature and is ubiquitously expressed in adult cells suggesting diverse physiological functions of this receptor.

500 µl

• Also Available: **$S1P_1$ Blocking Peptide** (10006616) 1 ea

$S1P_3$ Polyclonal Antibody 10006373

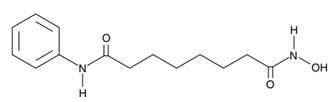
EDG-3, S1PR3, Sphingosine-1-Phosphate Receptor 3
Supplied as: Peptide affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human $S1P_3$ amino acids 12-25 • Host: rabbit • Cross Reactivity: (+) human, murine, and rat $S1P_3$ • Application(s): ICC and WB • $S1P_3$ is one of five GPCRs that are activated by S1P. It mediates S1P-induced cell proliferation, survival, migration, and related signaling events. $S1P_3$ is widely expressed in various tissues, suggesting diverse physiological functions of this receptor.

500 µl

SAHA 10009929

[149647-78-9] Suberoylanilide hydroxamic acid, Vorinostat, Zolinza™
MF: $C_{14}H_{20}N_2O_3$ **FW:** 264.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A HDAC inhibitor of class I and class II HDACs at around 50 nM; arrests cell growth in a wide variety of transformed cells in culture at 2.5-5.0 µM

50 mg
100 mg
250 mg
500 mg



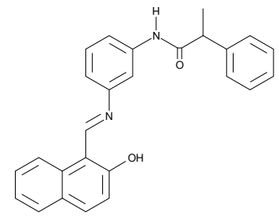
N1-hydroxy-N8-phenyl-octanediamide

• Also Available: **4-iodo-SAHA** (10495) 50 mg, 100 mg, 250 mg, 500 mg

Salermide 13178

[1105698-15-4]
MF: $C_{26}H_{22}N_2O_2$ **FW:** 394.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An inhibitor of SIRT1 and SIRT2, causing tumor-specific apoptotic cell death; causes 90% apoptosis within 72 hours (IC_{50} ~20 µM) by reactivating proapoptotic genes that are repressed by SIRT1 in MOLT4 leukemia cells

5 mg
10 mg
50 mg
100 mg

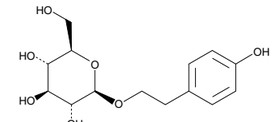


N-[3-[[(2-hydroxy-1-naphthalenyl)methylene]amino]phenyl]-a-methyl-benzeneacetamide

Salidroside 13628

[10338-51-9] Rhodioloside
MF: $C_{14}H_{20}O_7$ **FW:** 300.3 **Purity:** ≥97%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A glycoside isolated from plants used in Chinese medicine for a broad range of conditions; at 100 µM, significantly reduces apoptosis in response to H_2O_2 or cobalt chloride; protects mice from acetaminophen-induced toxicity

500 µg
1 mg
5 mg
10 mg

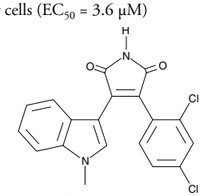


2-(4-hydroxyphenyl)ethyl-β-D-glucopyranoside

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



3-(2,4-dichlorophenyl)-4-(1-methyl-1H-indol-3-yl)-1H-pyrrole-2,5-dione

SB 415286 10010247

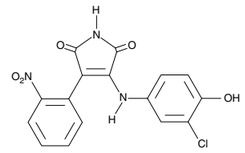
[264218-23-7]

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



3-[(3-chloro-4-hydroxyphenyl)amino]-4-(2-nitrophenyl)-1H-pyrrole-2,5-dione

SB 431542 13031

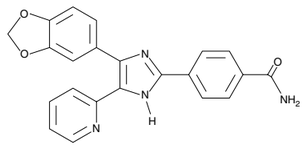
[301836-41-9]

MF: $C_{22}H_{18}N_4O_3$ **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



4-[4-(1,3-benzodioxol-5-yl)-5-(2-pyridinyl)-1H-imidazol-2-yl]-benzamide

SC-1 10009557

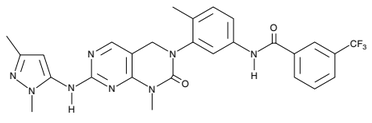
Pluripotin

MF: $C_{27}H_{25}F_3N_8O_2$ **FW:** 550.5 **Purity:** ≥98%

A crystalline solid **Stability:** ≥2 years at -20°C

Summary: A small molecule activator of stem cell renewal that allows the propagation of OG2 mES cells for at least 10 passages in an undifferentiated state; activity is mediated by the combined inhibition of RasGAP and ERK1 with K_d values of 98 and 212 nM, respectively

1 mg
5 mg
10 mg
25 mg



N-(3-(7-(1,3-dimethyl-1H-pyrazol-5-ylamino)-1-methyl-2-oxo-1,2-dihydropyrimido[4,5-d]pyrimidin-3(4H)-yl)-4-methylphenyl)-3-(trifluoromethyl) benzamide

SC-51089 10011561

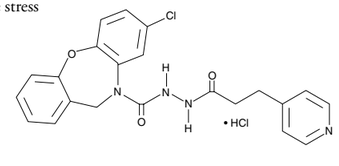
[146033-02-5] CID132748

MF: $C_{22}H_{19}ClN_4O_3$ • HCl **FW:** 459.3 **Purity:** ≥95%

A crystalline solid **Stability:** ≥2 years at -20°C

Summary: A selective EP_1 antagonist that displays analgesic activity in mice (ED_{50} = 6.3 mg/kg when given subcutaneously) and in rats; inhibits the growth of glioma cell lines *in vitro* (IC_{50} = ~1 µM) and slows tumor growth *in vivo*; attenuates neuronal cell death in response to oxidative stress

5 mg
10 mg
25 mg
50 mg



8-chloro-2-[1-oxo-3-(4-pyridinyl)propyl]hydrazide-dibenz[b,f][1,4]oxazepine-10(11H)-carboxylic acid, monohydrochloride

SET7/9 (human recombinant) 10320

KMT7, SETD7/9, SET Domain-containing Protein 7/9

Supplied as: A solution in 50 mM sodium phosphate, pH 7.2, containing 100 mM sodium chloride and 20% glycerol **Purity:** ≥95%

Stability: ≥6 months at -80°C

Summary: Source: recombinant N-terminal His-tagged SET7/9 amino acids 1-366, purified from *E. coli* · M_r: 43.3 kDa • SET7/9 is exclusively a mono-methylase that methylates histone H3, tumor suppressor p53, and transcription factor TAF10. SET7/9 was shown to catalyze methylation of p53 in response to DNA damage thereby activating p53 for subsequent acetylation. SET7/9 is able to modulate p53 activity in a human cancer cell line, implying that it may play a significant role in human tumorigenesis.

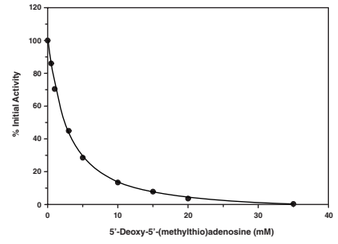
25 µg
50 µg
100 µg

SET7/9 Methyltransferase Inhibitor Screening Assay Kit 700270

Stability: ≥6 months at -80°C

Summary: SET7/9 is a MT that acts on various substrates including histone 3 at lysine residue 4 (H3K4), p53, and the transcription factor TAF 10. In Cayman's SET7/9 MT Inhibitor Screening Assay the transfer of the methyl group from SAM by SET7/9 to the acceptor peptide (TAF 10) generates SAH, which is rapidly converted to urate and H_2O_2 using an enzyme mixture provided in the kit. A subsequent reaction between H_2O_2 and ADHP produces the highly fluorescent compound resorufin.

96 wells



SET7/9 (FL) Polyclonal Antibody 13780

KMT7, SETD7/9, SET Domain-containing Protein 7/9

Supplied as: Protein-A purified IgG **Stability:** ≥1 year at -20°C

Summary: Antigen: human recombinant SET7/9 (amino acids 1-366) • Host: rabbit • Cross Reactivity: (+) human and murine SET7/9 • Application(s): WB • SET7/9 uses S-adenosylmethionine to methylate histone H3 and H4. Human SET7/9 is a 366 amino acid protein with observed migration on SDS-PAGE at 49 kDa.

500 µl

SET8 (human recombinant) 10319

PR-Set7, SETD8, SET Domain-containing (lysine methyltransferase) 8

Purity: ≥95%

Supplied as: A solution in 50 mM sodium phosphate, pH 7.2, containing 100 mM sodium chloride and 20% glycerol **Stability:** ≥6 months at -80°C

Summary: Source: recombinant N-terminal His-tagged SET8 amino acids 190-352, purified from *E. coli,* NP_065115 • M_r: 21.1 kDa • SET8 selectively mono-methylates histone H4 at lysine 20, an event proven to have an important role in chromatin structure and transcriptional activation. SET8 is also a novel regulator of p53, mono-methylating lysine 382 of the tumor suppressor. SET8's ability to suppress p53 transcriptional activity implies that it may play a significant role in tumorigenesis.

25 µg
50 µg
100 µg

SET8 Methyltransferase Inhibitor Screening Assay Kit 700350

PR-Set7, SETD8, SET Domain-containing (lysine methyltransferase) 8

Stability: ≥6 months at -80°C

Summary: SET8 is a MT that selectively mono-methylates histone H4 at lysine residue 20 (H4K20). In Cayman's SET8 MT Inhibitor Screening Assay, the transfer of the methyl group from SAM by SET8 to the acceptor peptide (H4K20) generates SAH, which is rapidly converted to urate and H_2O_2 using an enzyme mixture provided in the kit. A subsequent reaction between H_2O_2 and ADHP produces the highly fluorescent compound resorufin.

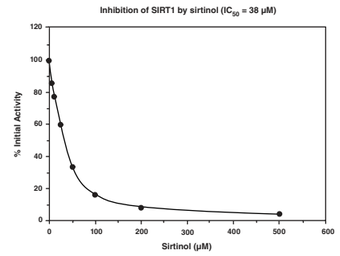
96 wells

SIRT1 Direct Fluorescent Screening Assay Kit 10010401

Stability: ≥6 months at -80°C

Summary: The sirtuins represent a distinct class of trichostatin A-insensitive lysyl-deacetylases (class III HDACs) that catalyze a reaction coupling lysine deacetylation to the formation of nicotinamide and O-acetyl-ADP-ribose. Cayman's SIRT1 Direct Fluorescent Screening Assay provides a fluorescence-based method for screening SIRT inhibitors or activators. The procedure requires only two easy steps, both performed in the same microplate. In the first step, the substrate is incubated with human recombinant SIRT along with its cosubstrate NAD⁺. Deacetylation sensitizes the substrate such that treatment with the developer in the second step releases a fluorescent product.

96 wells

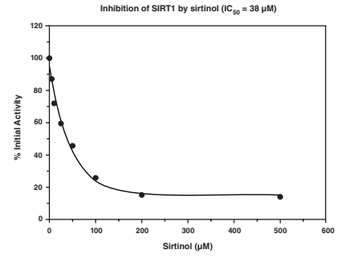


SIRT1 FRET-Based Screening Assay Kit 10010991

Stability: ≥6 months at -80°C

Summary: Cayman's SIRT1 FRET-based Screening Assay provides a novel fluorescence-based method for screening SIRT1 inhibitors or activators. The substrate, which is coupled to a fluorophore and quencher, is first incubated with human recombinant SIRT1. Deacetylation sensitizes the substrate such that treatment with a developer separates the quencher and fluorophore resulting in bright fluorescence.

96 wells



SIRT1 (human recombinant) 10011190

Sirtuin 1

Purity: ≥60%

Supplied as: A solution in 50 mM sodium phosphate, pH 7.2, containing 100 mM sodium chloride and 20% glycerol **Stability:** ≥9 months at -80°C

Summary: Source: recombinant N-terminal GST-fused SIRT1 amino acids 193-747 purified from *E. coli* • M_r: 89.2 kDa • SIRT1 is the human sirtuin with the greatest homology to yeast Sir2 and has been shown to regulate the activity of the p53 tumor suppressor and inhibit apoptosis.

25 units
50 units
100 units

SIRT2 (human recombinant) 10011191

Sirtuin 2

Purity: ≥90%

Supplied as: A solution in 50 mM sodium phosphate, pH 7.2, containing 100 mM sodium chloride and 20% glycerol **Stability:** ≥9 months at -80°C

Summary: Source: N-terminal His-tagged SIRT2 amino acids 2-389, purified from *E. coli* • M_r: 44.2 kDa • SIRT2 is a cytoplasmic protein responsible for the deacetylation of histone H4 and α-tubulin, a modification important for controlling the cell cycle. SIRT2 co-localizes with HDAC6 and microtubules and functions as a mitotic checkpoint in preventing chromosomal instability that can lead to hyperploid cells.

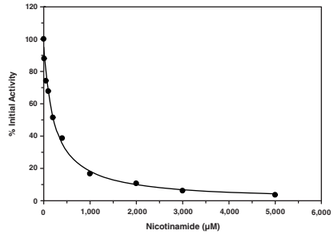
25 µg
50 µg
100 µg

SIRT3 Direct Fluorescent Screening Assay Kit 10011566

Stability: ≥6 months at -80°C

Summary: Cayman's Direct Fluorescent Screening Assay Kits provide a fluorescence-based method for screening SIRT3 inhibitors or activators. The procedure requires only two easy steps, both performed in the same microplate. In the first step, the substrate is incubated with human recombinant SIRT along with its cosubstrate NAD⁺. Deacetylation sensitizes the substrate such that treatment with the developer in the second step releases a fluorescent product.

96 wells



SIRT4 (human recombinant) 10317

Sirtuin 4

Purity: ≥85%

Supplied as: A solution in 50 mM sodium phosphate, pH 7.2, containing 100 mM sodium chloride, 2.5 mM DTT, and 20% glycerol **Stability:** ≥9 months at -80°C

Summary: Source: Recombinant N-terminal GST-tagged SIRT4, purified from *E. coli* • M_r: 61.9 kDa • SIRT4 is a mitochondrial ADP-ribosyltransferase responsible for the transfer of ADP-ribose from NAD to specific substrates such as glutamate dehydrogenase (GDH).

25 µg
50 µg
100 µg

SIRT5 (human recombinant) 10318

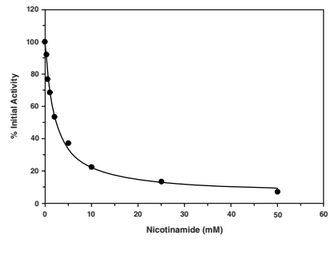
Sirtuin 5
Purity: ≥90%
Supplied as: A solution in 50 mM sodium phosphate, pH 7.2, containing 100 mM sodium chloride and 20% glycerol **Stability:** ≥9 months at -80°C
Summary: Source: Recombinant N-terminal GST-tagged SIRT4, purified from *E. coli* • M_r: 61.9 kDa • SIRT5 is located in the mitochondrial matrix and its functions are largely still being elucidated, however a few promising substrates have been studied. SIRT5 has been shown to deacetylate carbamoyl phosphate synthetase 1, activating the enzyme to catalyze the first step of the urea cycle.

25 µg
50 µg
100 µg

SIRT6 Direct Fluorescent Screening Assay Kit 700290

Stability: ≥6 months at -80°C
Summary: Cayman's Direct Fluorescent Screening Assays provide a fluorescence-based method for screening SIRT inhibitors or activators. The procedure requires only two easy steps, both performed in the same microplate. In the first step, the substrate is incubated with human recombinant SIRT along with its cosubstrate NAD^+. Deacetylation sensitizes the substrate such that treatment with the developer in the second step releases a fluorescent product.

96 wells



SIRT6 (human recombinant) 10315

Sirtuin 6
Purity: ≥95%
Supplied as: A solution in 25 mM Tris, pH 8.0, containing 100 mM sodium chloride and 20% glycerol **Stability:** ≥6 months at -80°C
Summary: Source: N-terminal His-tagged SIRT6 (amino acids 1-355) purified from *E. coli* • M_r: 43.7 kDa • SIRT6 associates specifically with telomeres and functions at chromatin to decrease NF-κB signaling. Mammalian cells depleted of SIRT6 display abnormal telomere structures similar to defects found in Werner syndrome, a premature aging disorder, and have a shortened life span.

25 µg
50 µg
100 µg

SIRT7 (human recombinant) 10316

Sirtuin 7
Purity: ≥85%
Supplied as: A solution in 50 mM sodium phosphate, pH 7.2, containing 100 mM sodium chloride, 5 mM DTT, and 20% glycerol **Stability:** ≥6 months at -80°C
Summary: Source: Full length (2-400 aa) recombinant N-terminal His-tagged SIRT7, expressed in *E. coli* • M_r: 49.3 kDa • SIRT7 activates transcription of RNA polymerase I and deacetylates p53. It prevents progressive deterioration of the heart, and is suggested to play an important role in regulation of stress responses and cell death in the heart.

25 µg
50 µg
100 µg

SIRT7 Polyclonal Antibody 13477

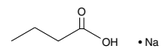
Sirtuin 7
Supplied as: Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human SIRT7 amino acids 35-51 and 361-377 • Host: rabbit • Cross Reactivity: (+) human SIRT7 • Application(s): WB • SIRT7 is a member of a family of proteins called sirtuins (Sir2-like proteins) and are present in prokaryotes and eukaryotes.

1 ea

Sodium Butyrate 13121

[156-54-7] Butyric Acid (sodium salt)
MF: $C_4H_8O_2$ • Na **FW:** 111.1 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at room temperature
Summary: A short chain fatty acid that inhibits HDACs, induces growth arrest, differentiation and apoptosis in cancer cells, and suppresses inflammation by reducing the expression of pro-inflammatory cytokines

50 g
100 g
250 g
500 g



butanoic acid, sodium salt

Sphingosine Kinase 1 (human recombinant) 10009236

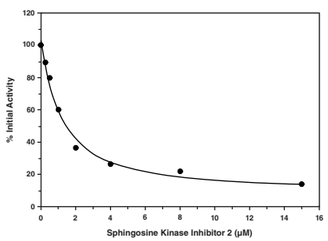
Purity: ≥80% by SDS-PAGE
Supplied in: 10 µg in 25 mM Tris-HCl, pH 8.0, containing 100 mM sodium chloride, 0.05% Tween 20, 50% glycerol, and 3 mM DTT
Stability: ≥6 months at -80°C
Summary: Source: human recombinant N-terminal His-tagged protein from Sf9 cells • M_r: 46.9 kDa • SPHK 1 catalyzes the phosphorylation of sphingosine to S1P. This reaction plays an important role in determining cell proliferation *versus* cell death.

1 ea

Sphingosine Kinase 1 Inhibitor Screening Assay Kit 700430

Stability: ≥6 months at -20°C
Summary: SPHK 1 and SPHK 2 phosphorylate D-*erythro*-sphingosine to yield S1P. S1P exhibits a broad spectrum of biological activities including cell proliferation, survival, migration, cytoskeletal organization, and morphogenesis. SPHK 1 is a potential therapeutic target for the control of cancer and inflammation. Cayman's SPHK 1 Inhibitor Screening Assay Kit provides a fluorescence-based method for screening SPHK 1 inhibitors.

96 wells



Sphingosine Kinase 1 Polyclonal Antibody 10006822

Supplied as: 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 murine SPHK 1, expected to react with rat SPHK 1 • Application(s): ICC and WB • SPHK 1 catalyzes the phosphorylation of sphingosine to S1P. This reaction plays an important role in determining cell proliferation *versus* cell death.

500 µl

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

Sphingosine Kinase 1 Polyclonal FITC Antibody 10012201

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

500 µl

Sphingosine Kinase 2 (human recombinant) 10009237

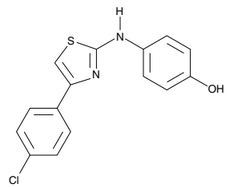
Purity: ≥80% by SDS-PAGE
Supplied in: 10 µg in 25 mM Tris-HCl, pH 8.0, 100 mM sodium chloride, 0.05% Tween 20, 50% glycerol, and 3 mM DTT
Stability: ≥6 months at -80°C
Summary: Source: human recombinant N-terminal His-tagged protein from Sf9 cells • M_r: 69.5 kDa • SPHK 2 catalyzes the phosphorylation of sphingosine to S1P. SPHK 2 is a potential therapeutic target for the control of cancer, inflammation, and other diseases.

1 ea

Sphingosine Kinase Inhibitor 2 10009222

[312636-16-1] SPHK II
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 with anti-proliferative activity; exhibits non-ATP-competitive inhibition of human recombinant GST-SPHK 1 with an IC_{50} value of 0.5 µM, with no inhibition against ERK2, PI3K, or PKCα at concentrations up to 60 µM; inhibits proliferation of human cancer cell lines (T-24, MCF-7, NCI/ADR, and MCF-7/VP) with IC_{50} values in the low µM range (0.9-4.6 µM)

5 mg
10 mg
25 mg
50 mg

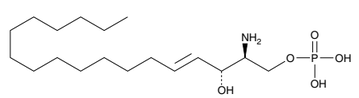


4-[[4-(4-chlorophenyl)-2-thiazolyl]amino]-phenol

Sphingosine-1-phosphate 62570

[26993-30-6] S1P
MF: $C_{18}H_{38}NO_5P$ **FW:** 379.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥1 year at -20°C
Summary: A potent lipid signaling molecule that exhibits a wide range of biological activities; it enhances cell growth and inhibits the normal apoptotic response to a variety of stimuli

1 mg
5 mg
10 mg
25 mg

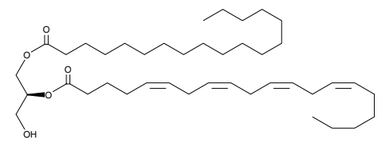


2S-amino-1-(dihydrogen phosphate)-4E-octadecene-1,3R-diol

1-Stearoyl-2-Arachidonoyl-*sn*-Glycerol 10008650

[65914-100096584-3] SAG
MF: $C_{41}H_{72}O_5$ **FW:** 645.0 **Purity:** ≥95%
A solution in acetonitrile **Stability:** ≥1 year at -80°C
Summary: Potently activates PKCα, PKCε, and PKCδ at nM concentrations; competitively binds to the Ras activator RasGRP (K_i = 4.49 µM) in Jurkat T-cells

1 mg
5 mg
10 mg
25 mg

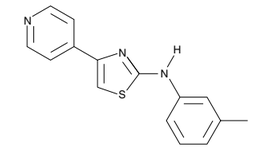


1-octadecanoyl-2-(5Z,8Z,11Z,14Z)-eicosatetraenoyl-sn-glycerol

STF-62247 13084

[315702-99-9]
MF: $C_{15}H_{13}N_3S$ **FW:** 267.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A small molecule that induces autophagy and selectively causes lethality in renal cell carcinoma cells that have lost the von Hippel-Lindau tumor suppressor activity (IC_{50} = 625 nM)

1 mg
5 mg
10 mg
25 mg

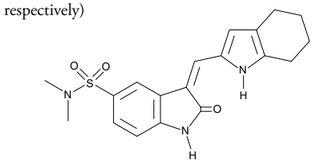


N-(3-methylphenyl)-4-(4-pyridinyl)-2-thiazolamine

SU 6656 13338

[330161-87-0]
MF: $C_{19}H_{21}N_3O_3S$ **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

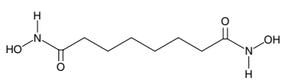


2,3-dihydro-N,N-dimethyl-2-oxo-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]-1H-indole-5-sulfonamide

Suberohydroxamic Acid 10574

[38937-66-5] SBHA, Suberic bis-Hydroxamic Acid
MF: $C_8H_{16}N_2O_4$ **FW:** 204.2 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A competitive HDAC inhibitor that has been shown to inhibit HDAC1 (IC_{50} = 0.25 µM) and HDAC3 (IC_{50} = 0.30 µM); causes cell differentiation, cell cycle arrest, or apoptosis

100 mg
250 mg
500 mg
1 g



N1,N8-dihydroxy-octanediamide

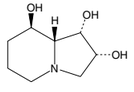
Receptor Tyrosine Kinase Inhibitors

Item No.	Item Name	Target	Effective Concentration
13653	ABT-869	VEGFR PDGFR	IC_{50} = range from 4-190 nM
10010248	AG-17	EGFR Kinase	IC_{50} = 460 µM in human epidermoid carcinoma A431 cells
10010300	AG-18	EGFR Kinase	IC_{50} = 35 µM in human epidermoid carcinoma A431 cells
10010312	AG-82	EGFR Kinase	IC_{50} = 3 µM in human epidermoid carcinoma A431 cells
10010313	AG-99	EGFR Kinase	IC_{50} = 10 µM in human epidermoid carcinoma A431 cells
10010314	AG-123	EGFR Kinase	IC_{50} = 2.4 µM in human epidermoid carcinoma A431 cells
10010315	AG-183	EGFR Kinase	IC_{50} = 0.8 µM in human epidermoid carcinoma A431 cells
10010568	AG-370	PDGFR kinase EGFR	IC_{50} = 20 µM in human bone marrow fibroblasts IC_{50} = 820 µM
10010311	AG-490	Jak-2	5 µM blocks growth of pre-B acute leukemia (ALL) cells
10010242	AG-494	EGFR Kinase	IC_{50} = 1 µM in HT- 22 cells
10010243	AG-825	Her-2/neu EGFR PDGFR	IC_{50} = 0.35 µM IC_{50} = 19 µM IC_{50} = 40 µM
10010592	AG-1296	PDGFR Kinase	IC_{50} = 0.4 µM (both *in vitro* and in Swiss 3T3 cells)
10010244	AG-1478	EGFR Kinase	IC_{50} = 3 nM
10010238	Erbstatin Analog	EGFR Kinase	IC_{50} = 0.14 µg/ml
10483	Erlotinib	EGFR	IC_{50} = 2.5 µM (murine recombinant) and 10 µM *(Xenopus)*
10005167	Genistein	Tyrosine-phosphorylation of histone H2B	
13166	Gefitinib	EGFR Kinase	IC_{50} = 0.2-0.4 µM in various cancer cell lines
10010329	HDBA	EGFR Kinase	IC_{50} = 0.012 µM
10008131	JNJ-10198409	PDGF-BB tyrosine kinase	IC_{50} = 4.2 nM
10010265	LFM-A13	BTK and Polo-like kinase	IC_{50} = 2.5 µM
10010422	Nilotinib	Bcr/Abl Tyrosine Kinase	IC_{50} = 15 nM in wild-type Bcr/Abl
13641	NVP-AEW541 (hydrochloride)	IGF-1R Kinase	IC_{50} = 0.086 µM
10010309	RG-13022	EGFR Kinase	IC_{50} = 1 µM in HT- 22 cells
10010310	RG-1462	EGFR Kinase	IC_{50} = 3 µM in HT- 22 cells
13337	ST638	Tyrosine phosphorylation	IC_{50} = 370 nM
13342	SU 5416	VEGFR-2 PDGFR	IC_{50} = 1 µM IC_{50} = 20 µM
13577	SU 11652	PDGFR-β VEGFR-2 FGFR1	IC_{50} = 3 nM IC_{50} = 27 nM IC_{50} = 170 nM

Swainsonine 16860

[72741-87-8] Tridolgosir
MF: $C_8H_{15}NO_3$ **FW:** 173.2 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An indolizidine alkaloid naturally found in certain plants that inhibits N-linked glycoside hydrolases, preventing the processing of asparagine-linked glycoproteins; reversibly inhibits lysosomal α-mannosidase and Golgi α-mannosidase II (IC_{50} = 0.2 µM); shown to have antiproliferative and antimetastatic effects of cancer cells in culture and in mice

1 mg
5 mg
10 mg
50 mg

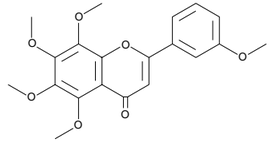


(1S,2R,8aR)-octahydro-indolizinetriol

Tangeritin 10009911

[481-53-8] NSC 53909, NSC 618905, Ponkanetin
MF: $C_{20}H_{20}O_7$ **FW:** 372.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A polymethoxylated flavone isolated from citrus peels; inhibits signaling in cancer cells, reducing ERK signaling in T47D breast cancer cells (IC_{50} ~3 µM)

1 mg
5 mg
50 mg
100 mg



5,6,7,8-tetramethoxy-2-(4-methoxyphenyl)-4H-1-benzopyran-4-one

TBLR1 Polyclonal Antibody 13788

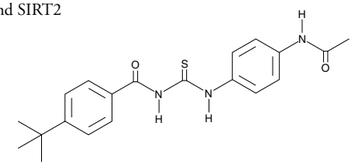
F-Box-Like/WD Repeat-Containing Protein, Tranducin β-Like 1X-Related Protein 1
Supplied as: Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: synthetic peptide from human TBLR1 within the region of amino acids 200-250 • Host: rabbit • Cross Reactivity: (+) human TBLR1 • Application(s): WB • TBLR1 is a WD-40 repeat protein that associates with nuclear receptor corepressor and silencing mediator of retinoid and thyroid hormone receptors, which are large protein complexes that play a role in transcriptional repression pathways.

1 ea

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 SIRT1 and SIRT2

5 mg
10 mg
50 mg
100 mg

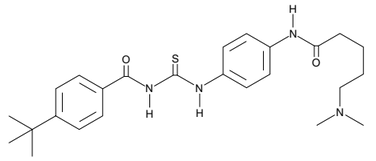


N-[[[4-(acetylamino)phenyl]amino]thioxomethyl-4-(1,1-dimethylethyl)]-benzamide

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: A water-soluble analog of tenovin-1; elevates p53 expression 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

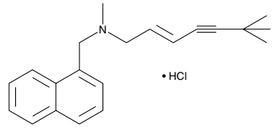


N-[[[4-[[5-(dimethylamino)-1-oxopentyl]amino]phenyl]amino]thioxomethyl]-4-(1,1-dimethylethyl)-benzamide

Terbinafine (hydrochloride) 10011619

[78628-80-5]
MF: $C_{21}H_{25}N$ • HCl **FW:** 327.9 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An antifungal compound clinically used to treat nail and skin infections; inhibits ergosterol synthesis at the stage of squalene epoxidation (IC_{50} = 30 nM for *C. albicans*); induces cell cycle arrest at the G_0/G_1 stage in COLO 205 tumor cells and human vascular endothelial cells

100 mg
250 mg
500 mg
1 g

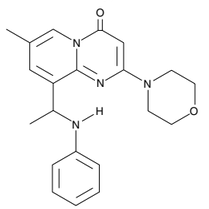


N-[(2E)-6,6-dimethyl-2-hepten-4-yn-1-yl]-N-methyl-1-naphthalenemethanamine, monohydrochloride

TGX-221 10007349

[663619-89-4]
MF: $C_{21}H_{24}N_4O_2$ **FW:** 364.4 **Purity:** ≥98%
A solution in ethanol **Stability:** ≥1 year at -20°C
Summary: A potent, selective, and cell permable inhibitor of PI3K p110β; IC_{50} increases from 5 to ~50 nM at ATP concentrations of 50 µM and 1 mM, respectively; inhibits PtdIns-(3,4)-P_2 production in platelets with an IC_{50} value of 50 nM

100 µg
500 µg
1 mg
5 mg



7-methyl-2-(4-morpholinyl)-9-[1-(phenylamino)ethyl]-4H-pyrido[1,2-a]pyrimidin-4-one

TIP60 Polyclonal Antibody 13789

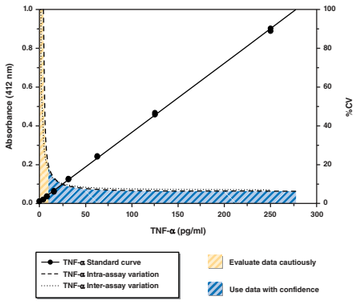
KAT5, Lysine Acetyltransferase 5
Supplied as: Protein A-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: synthetic peptide within the region of human TIP60 amino acids 480-530 • Host: rabbit • Cross Reactivity: human (isoform CRA_b), chimpanzee, orangutan, equine, canine, murine, ovine, rat, opossum, zebrafish, and *Xenopus* TIP60 • Application(s): IHC and WB • TIP60 belongs to the MYST family of HATs. It is a catalytic subunit of the NuA4 HAT complex which is involved in transcriptional activation of select genes principally by acetylation of nucleosomal histone H4 and H2A.

1 ea

TNF-α (human) EIA Kit 589201

Stability: ≥1 year at -20°C
Limit of Detection: 3.9 pg/ml
Summary: Cayman's TNF-α assay is an immunometric sandwich EIA that permits TNF-α measurements within the range of 0-250 pg/ml, typically with a limit of detection of 3.9 pg/ml. Inter- and intra-assay CV's of less than 5% can be achieved at most concentrations. This assay allows sensitive, specific analysis of TNF-α in serum or plasma.

96 wells
480 wells



TRAIL Polyclonal Antibody 160750

Apo-2L, TNF-related apoptosis-inducing ligand
Supplied as: IgG **Stability:** ≥1 year at 4°C
Summary: Antigen: human TRAIL amino acids 261-277 • Host: rabbit • Cross Reactivity: (+) human TRAIL • Application(s): WB • TRAIL is a type II membrane protein and is expressed in a variety of human tissues. TRAIL induces apoptosis and NF-κB activation in many tissues and cells.

500 µl

TRF2 Monoclonal Antibody (Clone 4A794.15) 13790

Telomeric Repeat Binding Factor 2, TERF2, TRBF2, TTAGGG Repeat Binding Factor 2
Supplied as: Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: full length human TRF2 • Host: mouse, clone 4A794.15 • Isotype: $IgG_{1κ}$ • Cross Reactivity: human, murine, muntjac, and rat TRF2 • Application(s): FC, ICC, and WB • TRF2 is a ubiquitously expressed protein that is implicated in the control of telomere length.

1 ea

TRF2 Polyclonal Antibody 13791

Telomeric Repeat Binding Factor 2, TERF2, TRBF2, TTAGGG Repeat Binding Factor 2
Supplied as: Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: full length human TRF2 • Host: goat • Cross Reactivity: human and murine TRF2 • Application(s): ChIP, ICC, IP, and WB • TRF2 is a ubiquitously expressed protein that is implicated in the control of telomere length.

1 ea

TRF4-1 Polyclonal Antibody 13792

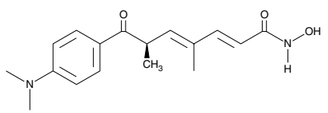
DNA Polymerase σ, DNA Polymerase κ, PAP-Associated Domain-Containing Protein 7
Suppled as: Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: synthetic peptide corresponding to human TRF4-1 amino acids 447-462 • Host: rabbit • Cross Reactivity: human TRF4-1 • Application(s): WB • TRF4-1 is a nuclear protein whose expression is cell cycle-regulated at a post-transcriptional level. Two genes TRF4-1 and TRF4-2, belonging to this family have been identified. TRF4 is also required to maintain a different aspect of higher order chromosome structure, sister chromatid cohesion.

1 ea

Trichostatin A 89730

[58880-19-6]
MF: $C_{17}H_{22}N_2O_3$ **FW:** 302.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥1 year at -20°C
Summary: A potent, reversible inhibitor of HDAC (IC_{50} = 70 nM)

500 µg
1 mg
5 mg
10 mg

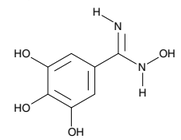


7-[4-(dimethylamino)phenyl]-N-hydroxy-4,6R-dimethyl-7-oxo-2E,4E-heptadienamide

Trimidox 10009083

[95933-74-7] VF 233
MF: $C_7H_8N_2O_4$ **FW:** 184.2 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A specific ribonucleotide reductase inhibitor; inhibits growth of human promyelocytic leukemia HL-60 cells (IC_{50} = 35 µM)

5 mg
10 mg
50 mg
100 mg



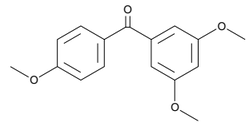
N-3,4,5-tetrahydroxy-benzenecarboximidamide

• Also Available: **Trimidox (hydrochloride)** (10011124) 5 mg, 10 mg, 25 mg, 50 mg

3,4',5-Trismethoxybenzophenone 10004185

[94709-12-3]
MF: $C_{16}H_{16}O_4$ **FW:** 272.3 **Purity:** ≥95%
A crystalline solid **Stability:** ≥1 year at -20°C
Summary: An analog of trimethoxy resveratrol; inhibits the growth of a variety of human tumor cell lines at concentrations from 0.4 to 2 µg/ml, which is 5-6 times more potent than resveratrol

10 mg
25 mg
50 mg
100 mg

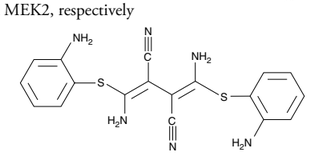


(3,5-dimethoxyphenyl)(4-methoxyphenyl)-methanone

U-0126 70970

[109511-58-2]
MF: $C_{18}H_{16}N_6S_2$ **FW:** 380.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A selective MAP Kinase Kinase (MKK, MEK) inhibitor with IC_{50} values of 72 and 58 nM for MEK1 and MEK2, respectively

1 mg
5 mg
10 mg
50 mg

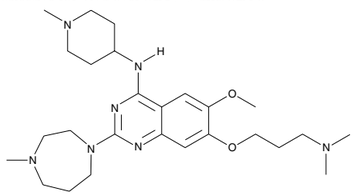


2,3-bis[amino[(2-aminophenyl)thio]methylene]-butanedinitrile

UNC0224 13631

[1197196-48-7]
MF: $C_{26}H_{43}N_7O_2$ **FW:** 485.7 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent and selective G9a HMTase inhibitor (IC_{50} = 15 nM, K_d = 29 nM); more than 1,000-fold selective for G9a over SET7/9 and SET8

1 mg
5 mg
10 mg
25 mg

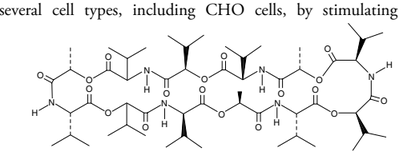


7-[3-(dimethylamino)propoxy]-2-(hexahydro-4-methyl-1H-1,4-diazepin-1-yl)-6-methoxy-N-(1-methyl-4-piperidinyl)-4-quinazolinamine

Valinomycin 10009152

[2001-95-8] NSC 122023
MF: $C_{54}H_{90}N_6O_{18}$ **FW:** 1,111.3 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A cyclododecadepsipeptide potassium-selective ionophore antibiotic; induces apoptosis in several cell types, including CHO cells, by stimulating potassium efflux

5 mg
10 mg
25 mg
50 mg

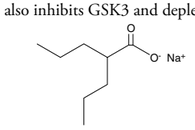


3,6,9,15,18,21,27,30,33-nonaisopropyl-12,24,36-trimethyl-1,7,13,19,25,31-hexaoxa-4,10,16,22,28,34-hexaaza-cyclohexatriacontane-2,5,8,11,14,17,20,23,26,29,32,35-dodecaone

Valproic Acid (sodium salt) 13033

[1069-66-5] 2-Propylvaleric Acid, Sodium Valproate
MF: $C_8H_{16}O_2$ • Na **FW:** 167.2 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An analog of valeric acid, long used as an anticonvulsant; inhibits class I HDACs with an IC_{50} value of ~2 mM; also inhibits GSK3 and depletes cellular IP_3

10 g
25 g
50 g
100 g

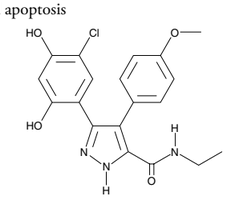


2-propyl-pentanoic acid, monosodium salt

VER-49009 13131

[940289-57-6]
MF: $C_{19}H_{18}ClN_5O_4$ **FW:** 387.8 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An Hsp90 inhibitor with an IC_{50} value of 47 nM; induces the expression of Hsp27 and Hsp72 while reducing the client proteins C-RAF, B-RAF, survivin, and PRMT5, causing cell cycle arrest and apoptosis

500 µg
1 mg
5 mg
10 mg

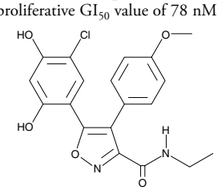


3-(5-chloro-2,4-dihydroxyphenyl)-N-ethyl-4-(4-methoxyphenyl)-1H-pyrazole-5-carboxamide

VER-50589 13132

[747413-08-7]
MF: $C_{19}H_{17}ClN_2O_5$ **FW:** 388.8 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An isoxazole compound that inhibits Hsp90 with an IC_{50} value of 21 nM; produces a mean cellular antiproliferative GI_{50} value of 78 nM when tested against a human cancer cell line panel

500 µg
1 mg
5 mg
10 mg

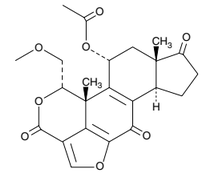


5-(5-chloro-2,4-dihydroxyphenyl)-N-ethyl-4-(4-methoxyphenyl)-3-isoxazolecarboxamide

Wortmannin 10010591

[19545-26-7] KY 12420
MF: $C_{23}H_{24}O_8$ **FW:** 428.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent, cell-permeable, and irreversible inhibitor of PI3K enzymes (IC_{50} = 1-10 nM)

1 mg
5 mg
10 mg
25 mg

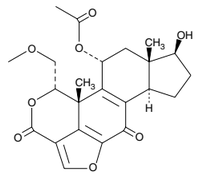


11-(acetyloxy)-1S,6bR,7,8,9aS,10,11R,11bR-octahydro-1-(methoxymethyl)-9a,11b-dimethyl-3H-furo[4,3,2-de]indeno[4,5-h]-2-benzopyran-3,6,9-trione

17β-hydroxy Wortmannin 13812

MF: $C_{23}H_{26}O_8$ **FW:** 430.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An analog of wortmannin; irreversibly binds PI3K; inhibits recombinant PI3K and mTOR (IC_{50} = 2.7 and 193 nM, respectively) and prevents the growth of LNCap cells (IC_{50} = 1.46 µM)

500 µg
1 mg
5 mg
10 mg

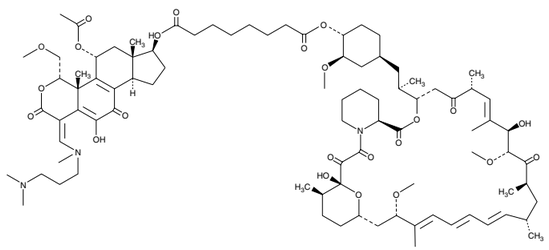


17β-hydroxy-11-(acetyloxy)-1S,6bR,7,8,9aS,10,11R,11bR-octahydro-1-(methoxymethyl)-9a,11b-dimethyl-3H-furo[4,3,2-de indeno[4,5-h]-2-benzopyran-3,6,9-trione

Wortmannin-Rapamycin Conjugate 13671

MF: $C_{88}H_{131}N_3O_{23}$ **FW:** 1,598.9 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: Consists of analogs of 17-hydroxy wortmannin and rapamycin conjugated *via* a prodrug linker, which are released upon hydrolysis of the prodrug linker *in vivo*; inhibits the growth of tumors in mice better than rapamycin alone

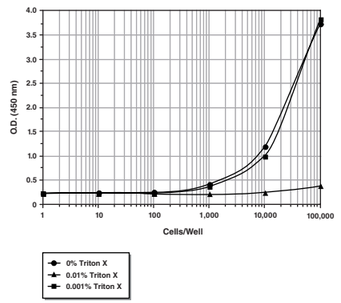
500 µg
1 mg
5 mg
10 mg



WST-1 Cell Proliferation Assay Kit 10008883

Stability: ≥1 year at -20°C
Summary: Cayman's WST-1 Proliferation Assay is based on the reduction of tetrazolium salt WST-1 to soluble formazan by electron transport across the plasma membrane of dividing cells. This kit will also allow investigators to screen drug candidates involved in cell cycle regulation.

96 wells
480 wells
4,800 wells

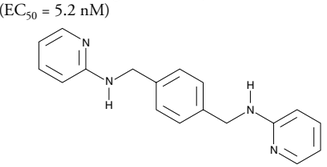


- Also Available: **MTT Cell Proliferation Assay Kit** (10009365)
  480 wells
  2,400 wells
  WST-8 Cell Proliferation Assay Kit (10010199)
  96 wells
  480 wells
  4,800 wells
  XTT Cell Proliferation Assay Kit (10010200)
  96 wells
  480 wells
  4,800 wells

WZ811 13639

[55778-02-4]
MF: $C_{18}H_{18}N_4$ **FW:** 290.4 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent inhibitor of binding of an SDF-1 peptide mimic to CXCR4 (EC_{50} = 0.3 nM); prevents CXCR4/SDF-1-mediated modulation of cAMP (EC_{50} = 1.2 nM) in cells; blocks SDF-1-induced Matrigel invasion by MDA-MB-231 human breast adenocarcinoma cells (EC_{50} = 5.2 nM)

1 mg
5 mg
10 mg
25 mg

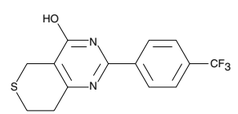


N1,N4-di-2-pyridinyl-1,4-benzenedimethanamine

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 APC-deficient colorectal cancer cells at 0.33 µM

1 mg
5 mg
10 mg
25 mg

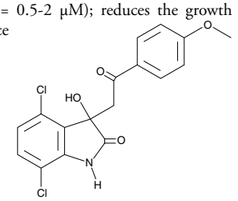


3,5,7,8-tetrahydro-2-[4-(trifluoromethyl)phenyl]-4H-thiopyrano[4,3-d]pyrimidin-4-one

YK-4-279 13661

[1037184-44-3]
MF: $C_{17}H_{13}Cl_2NO_4$ **FW:** 366.2 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: Blocks binding of RNA helicase A to ES-FLI1; induces apoptosis of Ewing's sarcoma tumor cells (IC_{50} = 0.5-2 µM); reduces the growth of Ewing's sarcoma orthotopic xenografts in mice

1 mg
5 mg
10 mg
50 mg

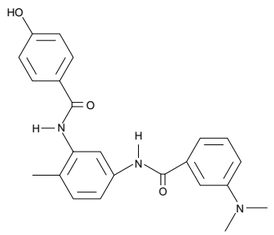


4,7-dichloro-1,3-dihydro-3-hydroxy-3-[2-(4-methoxyphenyl)-2-oxoethyl]-2H-indole-2-one

ZM 336372 10010367

[208260-29-1]
MF: $C_{23}H_{23}N_3O_3$ **FW:** 389.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent ATP-competitive inhibitor of Raf-1 *in vitro* (IC_{50} = 70 nM) with the paradoxical effect of inducing >100-fold activation of Raf-1 in whole cells; activates the Raf-1 signaling pathway in human carcinoid tumor cells resulting in suppression of cellular proliferation

1 mg
5 mg
10 mg
25 mg

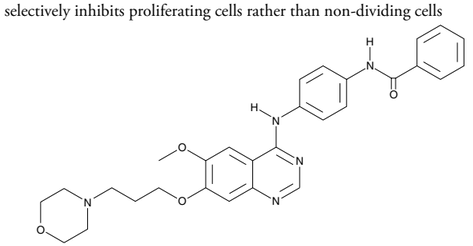


3-(dimethylamino)-N-[3-[(4-hydroxybenzoyl)amino]-4-methylphenyl]-benzamide

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} = 50nM), 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
100 mg



N-[4-[[6-methoxy-7-[3-(4-morpholinyl)propoxy]-4-quinazolinyl]amino]phenyl]-benzamide

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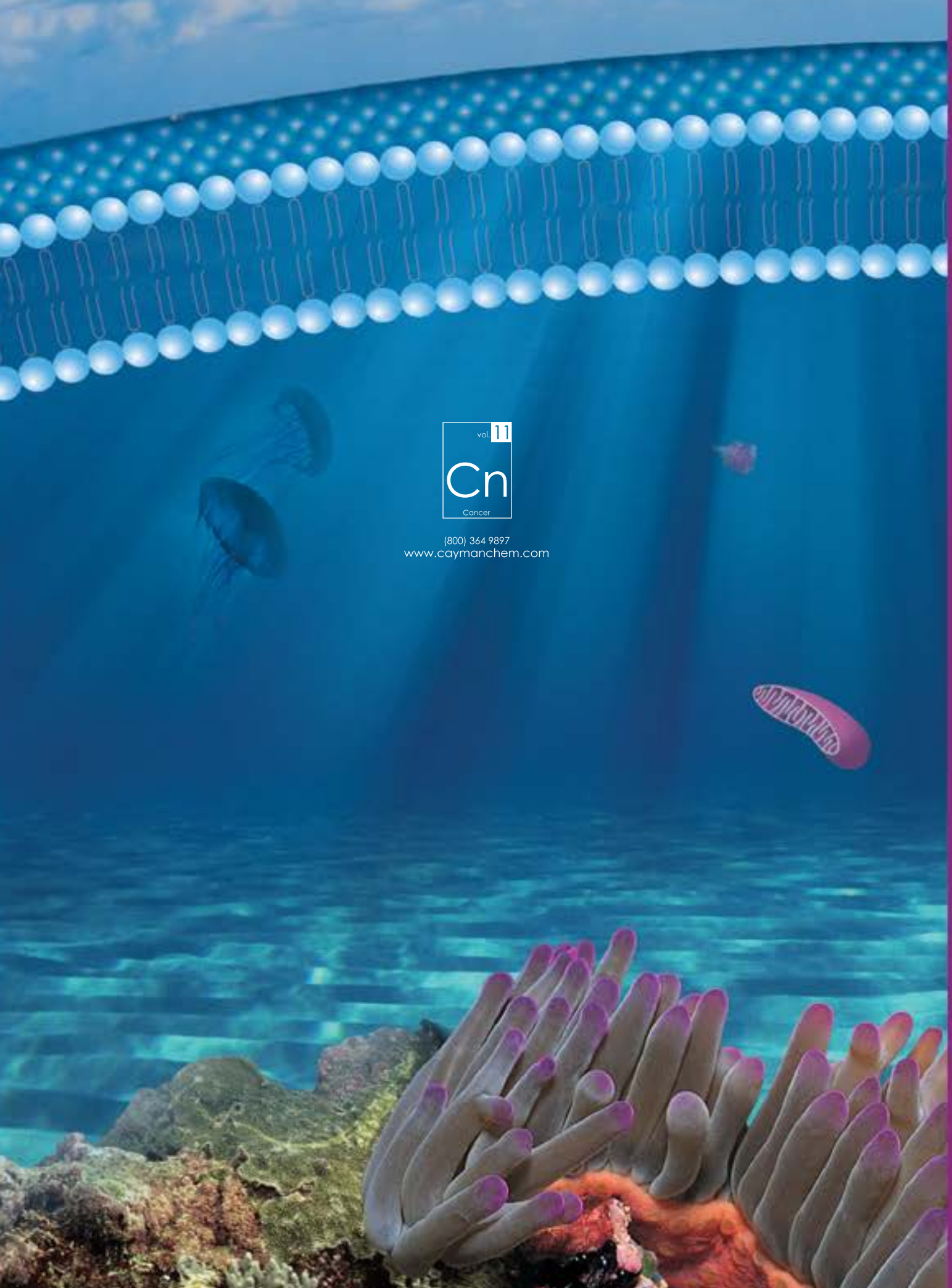
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