
INFLAMMATION
Cayman
CHEMICAL

Thomas G. Brock, Ph.D.

Introduction to Inflammation

Do cephalopods, like the octopus, have an inflammatory response? Very little is known about the cephalopod immune response, which is remarkable given the importance of these creatures to the sushi business. However, cephalopods are large invertebrates and much can be gleaned from the growing literature on the inflammatory response of this diverse group. Even the lowly fruitfly has hematopoiesis, although the primary immune cell is the hemocyte. Subsets of hemocytes, phagocytose bacteria and apoptotic bodies, generate defensins and contribute to wound repair and clotting mechanisms. The toll-like receptors, well known in mammalian systems for their role in immunity, were named for their homology to the Toll receptors of *Drosophila*, receptors that activate cellular immunity as well as the systemic production of antimicrobial peptides. Infection of our good friend the octopus with the coccidian *Aggregata octopiana* produces some classical features of an immune response, including increased cellularity as hemocytes surround sporocysts, phagocytose many of these, and form granuloma-like structures around persistent parasites.

In humans, inflammation is an important topic that is growing with the aging of the population. In the recent past, emphasis has been on treating the pain side of inflammation and, of course, the value of the pain relief market is staggering. With increasing public awareness of the importance of inflammation in aging, pathogenesis, and pain production, there is a growing market for products that prevent inflammation. This is, in part, typified by the growing use of natural compounds as 'nutraceuticals', even though their actual therapeutic effects may be poorly understood. Clearly, there is an immediate need for research in these areas.

Cayman's goal is to make that research possible. Within this catalog, we include many of our products that are related to inflammation research. Additional chemicals, assay kits, recombinant proteins, and antibodies can be found at our website, Caymanchem.com. We also encourage you to contact us to discuss what products or services we can provide to further help make your research successful.

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abbreviations

cAMP	Adenosine 3′,5′-cyclic monophosphate
BLT	Leukotriene B Receptor
BSA	Bovine Serum Albumin
CB	Cannabinoid
COX	Cyclooxygenase
CRTH2	Chemoattractant Receptor-homologous Molecule Expressed on Th2 Cells
CYP450	Cytochrome P450
CysLT	Cysteinyl Leukotriene
DHA	Docosahexaenoic Acid
DP	D-type Prostanoid Receptor
DTNB	5,5′-Dithio-*bis*-(2-nitrobenzoic acid); Ellman's Reagent
DTT	Dithiothreitol
EDTA	Ethylenediaminetetraacetic Acid
EIA	Enzyme Immunoassay
EP	Prostaglandin E_2 Receptor
EPA	Eicosapentaenoic Acid
FAAH	Fatty Acid Amide Hydrolase
FC	Flow Cytometry
FITC	Fluorescein Isothiocyanate
FP	Prostaglandin $F_{2\alpha}$ Receptor
FPIA	Fluorescence Polarization Immunoassay
cGMP	Guanosine 3′,5′-cyclic monophosphate
GPCR	G Protein-Coupled Receptor
H_2S	Hydrogen Sulfide
ICC	Immunocytochemistry
IgG	Immunoglobulin G
IHC	Immunohistochemistry
IL	Interleukin
IP	Immunoprecipitation
LO	Lipoxygenase
LPS	Lipopolysaccharide
LT	Leukotriene
LX	Lipoxin
MPO	Myeloperoxidase
NF-κB	Nuclear Factor-κB
NO	Nitric Oxide
NOS	Nitric Oxide Synthase
NSAID	Non-steroidal Anti-inflammatory Drug
PAF	Platelet-Activating Factor
PAF-AH	PAF Acetylhydrolase
PBS	Phosphate Buffered Solution
PDE	Phosphodiesterase
PE	Phycoerythrin
PG	Prostaglandin
PGES	Prostaglandin E Synthase
PL	Phospholipase
$cPLA_2$	Calcium-dependent Cytosolic Phospholipase A_2
$iPLA_2$	Calcium-independent Phospholipase A_2
$sPLA_2$	Secretory Phospholipase A_2
PMNL	Polymorphonuclear Leukocyte
PPAR	Peroxisome Proliferator-activated Receptor
PUFA	Polyunsaturated Fatty Acid
S1P	Sphingosine-1-phosphate
SRS-A	Slow-Reacting Substance of Anaphylaxis
TMPD	N,N,N′,N′-Tetramethyl-p-Phenylenediamine
TNF-α	Tumor Necrosis Factor-α
TNFR	Tumor Necrosis Factor Receptor
TP	Thromboxane Receptor
TX	Thromboxane
VR	Vanilloid Receptor
WB	Western Blot

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Bromodomains and Inflammation – An Emerging Interface

A recent tour-de-force publication in Nature introduced a synthetic histone mimic that suppressed inflammatory gene expression in both isolated cells and in mice.[1] The histone mimic, called I-BET, prevents the binding of certain bromodomain-containing proteins (BETs, for bromodomain and extra terminal domain) to histones, selectively blocking the expression of some genes induced by lipopolysaccharide (LPS). While the study itself is worth examining more closely, it also invites a consideration of epigenetics, histone acetylation, and bromodomains in the context of inflammation. This article touches on these topics.

Epigenetics and Inflammation

Epigenetics can be defined as the study of heritable changes in gene expression that do not involve changes in DNA sequence or copy number. Usually implicit in this concept is that the changes are passed through several cell divisions and, in some cases, maintained through sexual reproduction to affect processes in offspring. For example, epigenetic changes drive the differentiation of stem cells into specialized cells and the morphogenesis of discrete organs. Another example comes from imprinted genes, genes whose expression is determined by the parent that contributed them. Thus, the allele for insulin-like growth factor-2 (IGF2) that is inherited from the father is expressed, while that from the mother is not. The difference in expression is thought to be due, at least in part, to methylation of DNA that occurs in male-, but not female-derived, alleles.[2] DNA methylation, then, is an example of an epigenetic mechanism for changing gene expression that can be stable through multiple cell divisions and, in some cases, through reproduction.

More recently, epigenetics is commonly taken to include all changes in gene expression that result from changes in the nucleosome, regardless of duration. The nucleosome, of course, is the basic structural unit of chromatin, consisting of a short stretch of DNA wrapped twice around a protein octamer composed of two sets of the core histones, H2A, H2B, H3, and H4. Previously, the histones were thought to have a passive role, organizing chromatin by serving as a spool around which the thread of DNA can be wound. Now, it is clear that the nucleosome is a sophisticated device for tying down or feeding out genetic material and in this way, regulating transcription. Each histone has an N-terminal tail extending from the central globular domain (Figure 1). These tails are studded with basic residues (lysine, arginine) at regular intervals. Each basic side chain can potentially interact with the negatively-charged phosphate backbone of the adjacent DNA, defining a physical interaction that binds the thread to the spool. That is, unmodified lysines and arginines can clamp down on DNA, preventing its access to promoters. The positive charges can be altered by acetylation. In addition, serines, threonines, and tyrosines can be phosphorylated, adding negative charges to specific histones and altering the DNA interaction. All of these changes are reversible and many are short-lived.

In some ways, inflammation parallels epigenetics. Inflammation can be chronic, persisting for months or years, suggestive of persistent epigenetic changes. Inflammation can be acute, involving an immune response lasting only hours or days, with transient changes in histone marks being the only "epigenetic" process. Moving beyond this over-simplified dichotomy, different types of inflammatory processes can have distinct epigenetic 'signatures'. A gram-negative bacterial infection can generate an endotoxin-initiated cytokine storm, with gene expression impacted, only in part, by histone modification on select nucleosomes.[1] Compare this with hypomethylation of DNA associated with alcohol-induced oxidative stress during liver disease, the hypermethylation of CpG islands following kidney damage or viral infection, or histone acetylation accompanying rheumatoid

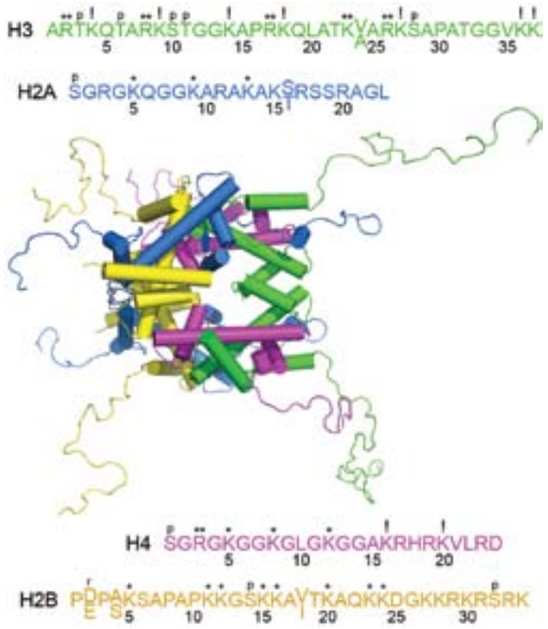

Figure 1. Histone tails. The amino termini project from the octamer core. N-terminal sequences for each type of histone are given, with known sites of acetylation (*), methylation (**), either acetylation or methylation (!), or phosphorylation (p) indicated.

arthritis.[3-5] Quite possibly, both short- and long-term epigenetic changes occur during a limited inflammatory event, with the long-term changes setting the stage for subsequent disease, like cancer.[4,6]

Histone Acetylation and Bromodomains

Histone acetyltransferases (HATs) add acetyl groups to basic residues on proteins, while histone deacetylases (HDACs) remove them. HATs commonly work as part of multimeric complexes. For example, the protein GCN5 associates with TATA-binding protein (TBP) and TBP-associated factors (TAF) as part of the TBP-free TAF complex (TFTC), providing HAT activity that activates transcription. GCN5 also is part of an SPT3-TAF9-GCN5 acetyltransferase (STAGA) complex and the ADA2A-containing complex (ATAC), both of which act as transcriptional co-activators. HAT-containing complexes can act in at least four broad ways.[7,8] First, they affect general chromosome structure through global histone acetylation. Second, they can act as co-activators of specific genes by docking near transcription start sites and acetylating histone tails. These acetylated sites then allow binding of ATP-dependent chromatin-remodeling complexes, accommodating transcription. In a third, related process, HAT complexes act as co-activators by hyperacetylating histones near specific start sites. As basic amino acids on the histone core are integral in maintaining histone-DNA binding, hyperacetylation causes histone eviction and chromatin opening, allowing the recruitment of additional factors to drive transcription (Figure 2). Finally, HATs can directly acetylate and activate transcription factors and other proteins involved in initiating transcription. Because they target proteins other than histones, most HATs have alternative names indicating that they are lysine ATs, or KATs. Thus, GCN5 is also called KAT2A.

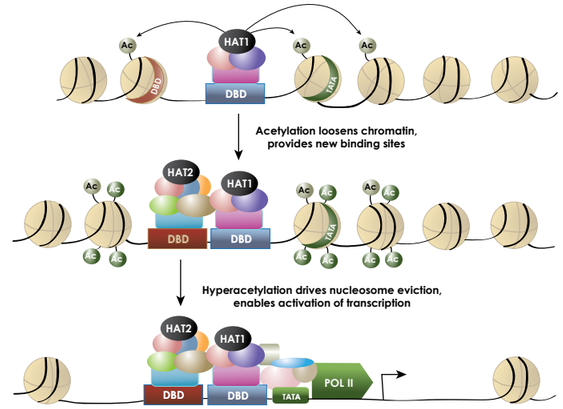

Figure 2. Some HATs associate with DNA as part of a multimeric complex. DNA targeting depends on one member of the complex containing a specific DNA binding domain (DBD). Localized acetylation of histone tails loosens chromatin and provides additional potential binding sites. Other HAT-containing complexes may then attach and hyperacetylate histones, resulting in nucleosome eviction that opens additional binding sites, facilitating the initiation of transcription.

HDACs, like HATs, modulate transcription. They often participate in the formation of transcriptional repressor complexes, inducing chromatin compaction through histone deacetylation, and silencing gene expression. Their actions are targeted to specific DNA sequences and histone marks, by associated adapter proteins or transcription factors that target conserved DNA binding domains (DBD) or specific histone modifications. For example, certain HDACs form a complex with unactivated PPARγ, binding to the PPARγ DBD, and actively suppress gene expression. Activation of PPARγ leads to shedding of the HDAC complex followed by recruitment of a HAT complex, followed by acetylation-dependent chromatin relaxation and transcription.[9] Like HATs, there are several types of HDACs, each having specific binding partners and functions. Cayman carries a broad collection of recombinant enzymes, functional assay kits, and high purity reagents for the study of HATs and HDACs.

Lysine acetylation is one kind of histone mark targeted by certain proteins. Like putting a new tooth on a key, it changes the proteins that it can interact with. After acetylation, the long side chain of lysine becomes a perfect fit for a bromodomain, a region of about 70 amino acids that form a multi-helix bundle (Figure 3). That is, lysine acetylation creates a docking site for over 40 proteins in humans. Nine of these have enzymatic activity, acting as HATs, methyltransferases, kinases, or ubiquitin ligases. The others are adapters, linking protein complexes to nucleosomes to regulate chromatin structure and gene expression. Most are 700 to 3,500 amino acids in length, so they are 10-50 times larger than the bromodomain. As a point of perspective, the histone octamer core of each nucleosome totals about 800 amino acids. Bromodomain-containing proteins alone, then, are physically significant structures relative to nucleosomes. Since many act as co-activators of transcription, one might envision them as helping to forcibly unwind compacted chromatin, increasing the availability of stretches of DNA to transcriptional enzymes.

BET Proteins and Inflammation

The BET family of proteins includes BRD2, BRD3, and BRD4, proteins that are central to the assembly of histone acetylation-dependent chromatin complexes that regulate inflammatory gene expression.[10,11] As indicated above, their roles in LPS-mediated gene expression were revealed by a recent study using I-BET, a potent and competitive inhibitor of BET protein binding to acetylated histone.[1] As might be expected, LPS induced the expression of several hundred genes in bone-marrow derived macrophages (BMDMs). I-BET suppressed the expression of a subset of these genes, including key LPS-inducible cytokines and chemokines, including IL-6, Ifnβ1, IL-1β, IL-12α, Cxcl9, and Ccl12. I-BET didn't simply disrupt LPS signaling, since several pro-inflammatory genes that were induced by LPS, including TNF-α, were unaffected by I-BET. Importantly, LPS caused BET accumulation at the transcriptional start sites of I-BET suppressible genes, and I-BET blocked this. Finally, I-BET protected mice from LPS- or *Salmonella*-triggered cytokine expression and mortality, suggesting that drugs that interfere with epigenetic signaling have therapeutic potential. I-BET is available from Cayman as item no. 10676.

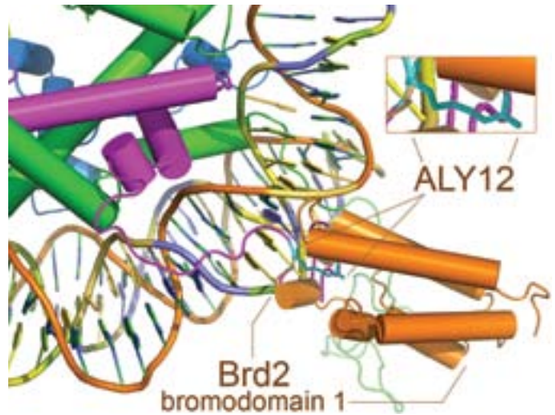

Figure 3. The 73 amino acid bromodomain 1 of Brd2 forms a multi-helix structure that grips acetylated lysine 12 (ALY12), presented on the tail of histone 4 (magenta) near DNA circling the histone octamer.

References

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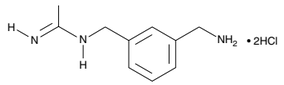
1400W (hydrochloride) 81520

[214358-33-5]
MF: $C_{10}H_{15}N_3$ • 2HCl **FW:** 250.2 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent, selective inhibitor of iNOS with K_i values of 7 nM, 2 µM, and 50 µM for iNOS, nNOS, and eNOS, respectively

5 mg
10 mg
50 mg
100 mg



N-Ac-Tyr-Val-Ala-Asp-CMK 10014

[178603-78-6] Ac-YVAD-CMK
MF: $C_{24}H_{33}ClN_4O_8$ **FW:** 541.0 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A selective, irreversible inhibitor of IL-1β converting enzyme (ICE; caspase-1)

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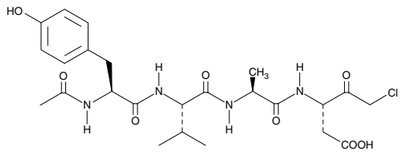
1 mg
5 mg
10 mg



N-Ac-Tyr-Val-Ala-Asp-CHO 10016

[14413-51-3] Ac-YVAD-CHO
MF: $C_{23}H_{32}N_4O_8$ **FW:** 492.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A selective inhibitor of IL-1β converting enzyme (ICE; caspase-1)

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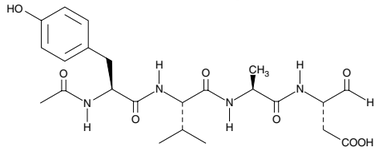
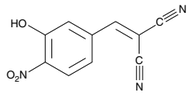


AG-126 13297

[118409-62-4] Tyrphostin AG-126
MF: $C_{10}H_5N_3O_3$ **FW:** 215.2 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A tyrphostin that is a poor inhibitor of EGFRK (IC_{50} = 450 µM) and PDGFRK (IC_{50} > 100 µM) which has been found to inhibit the phosphorylation of ERK1 and ERK2 at 25-50 µM; blocks the production of TNF-α, attenuating signaling through NF-κB, the induced expression of COX-2 and iNOS, and the inflammatory response

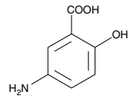
1 mg
5 mg
10 mg
25 mg



5-Aminosalicylic Acid 70265

[89-57-6] 5-ASA
MF: $C_7H_7NO_3$ **FW:** 153.1 **Purity:** ≥99%
A crystalline solid **Stability:** ≥1 year at -20°C
Summary: A metabolite and potential pharmacologically active component of sulphasalazine, a drug used in the treatment of Crohn's disease and ulcerative colitis

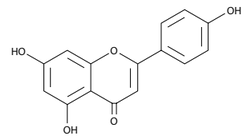
10 g
25 g
50 g
100 g



Apigenin 10010275

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

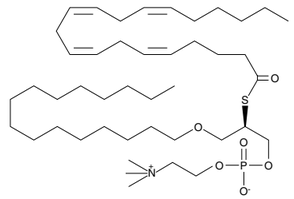
25 mg
50 mg
100 mg
500 mg



Arachidonoyl thio-PC 62240

[146797-82-2] 2-deoxy-2-thio Arachidonoyl PC
MF: $C_{44}H_{82}NO_6PS$ **FW:** 784.2 **Purity:** ≥98%
A solution in ethanol containing 0.1% BHT **Stability:** ≥2 years at -20°C
Summary: A chromogenic substrate for many PLA_2s including $sPLA_2$, $cPLA_2$, and $iPLA_2$

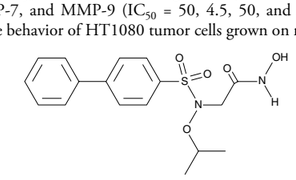
5 mg
10 mg
25 mg
50 mg



ARP 100 13321

[704888-90-4] CAY10609, MMP-2 Inhibitor III
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 matrix metalloproteinase-2 (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

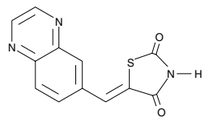
1 mg
5 mg
10 mg
25 mg



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 PI3-kinase γ 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



• Also Available: **AS-605240 (potassium salt)** (9000980)

AT-56 13160

[162640-98-4]
MF: $C_{25}H_{27}N_5$ **FW:** 397.5 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A selective, competitive, and highly bioavailable inhibitor of L-PGDS (K_i = 75 µM); inhibits the production of PGD_2 by L-PGDS purified from human CSF and recombinant murine cells with an IC_{50} value of 95 µM

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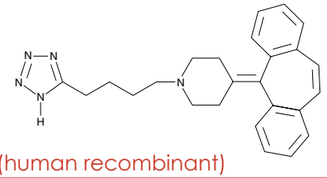
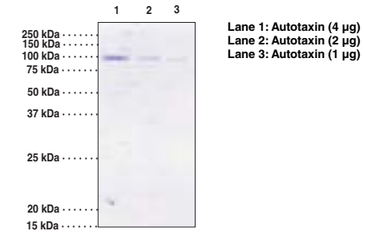
5 mg
10 mg
50 mg



Autotaxin (human recombinant) 10803

ATX Ectonucleotide Pyrophosphatase/Phosphodiesterase-2, ENPP-2, Lysophospholipase D
M_r: 98.8 kDa **Purity:** ≥95%
Supplied in: 50 mM Tris-HCl, pH 8.0, containing 150 mM sodium chloride and 20% glycerol
Summary: Recombinant C-terminal histidine-tagged protein expressed using a baculovirus overexpression system in *Sf*21 cells • ATX is a secreted lysophospholipase D that catalyzes the hydrolysis of LPC to generate LPA; ATX-LPA signaling is involved in a range of pathologies including tumor progression and inflammation.

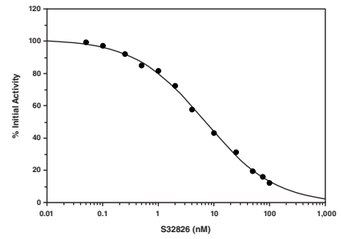
5 µg
10 µg
25 µg



Autotaxin Inhibitor Screening Assay Kit 700580

ATX Ectonucleotide Pyrophosphatase/Phosphodiesterase-2, ENPP-2, Lysophospholipase D
Stability: ≥6 months at -80°C
Summary: Autotaxin is a secreted lysophospholipase D that catalyzes the hydrolysis of LPC to generate LPA. LPA is a lipid mediator that activates GPCRs and induces a variety of biological responses, such as neurogenesis, angiogenesis, smooth-muscle contraction, platelet aggregation, and wound healing. ATX-LPA signaling is involved in a range of pathologies including tumor progression and inflammation. Cayman's Autotaxin Inhibitor Screening Assay provides a convenient method for screening human ATX inhibitors. In this assay ATX cleaves *bis*-(*p*-nitrophenyl) phosphate liberating *p*-nitrophenol, a yellow product that is measured at 405-415 nm.

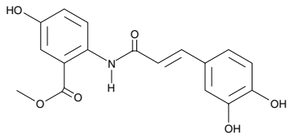
96 wells



Avenanthramide-C methyl ester 10011336

[955382-52-2]
MF: $C_{17}H_{15}NO_6$ **FW:** 329.3 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: Inhibitor of NF-κB activation that blocks the phosphorylation of IKK and IκB (IC_{50} ~40 µM); dose dependently inhibits the expression and secretion of IL-6, IL-8, and MCP-1 in human aortic endothelial cells

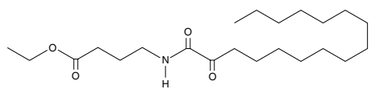
500 µg
1 mg
5 mg
10 mg



AX 048 13823

[873079-69-7]
MF: $C_{22}H_{41}NO_4$ **FW:** 383.6 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent group IVA $cPLA_2$ inhibitor (X_i(50) = 0.022); reduces thermal hyperalgesia evoked by carrageenan injection of rat hind paw (ED_{50} = 1.2 mg/kg); does not inhibit COX activity or interfere with CB_1 receptor signaling

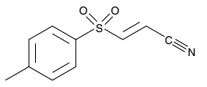
500 µg
1 mg
5 mg
10 mg



BAY-11-7082 10010266

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

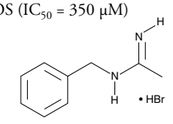
5 mg
10 mg
25 mg
50 mg



N-Benzylacetamidine (hydrobromide) 13570

[186545-76-6]
MF: $C_9H_{12}N_2$ • HBr **FW:** 229.1 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent inhibitor of iNOS (IC_{50} = 0.20 µM), with over 1,000-fold selectivity compared to eNOS (IC_{50} = 350 µM)

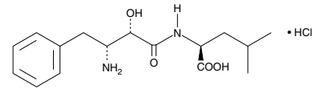
5 mg
10 mg
50 mg
100 mg



Bestatin (hydrochloride) 70520

[65391-42-6]
MF: $C_{16}H_{24}N_2O_4$ • HCl **FW:** 344.8 **Purity:** ≥99%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An inhibitor of aminopeptidases and a potent, irreversible inhibitor of LTA_4 hydrolase (K_i = 201 nM)

5 mg
10 mg
50 mg
100 mg



BLT_1 Receptor Monoclonal Antibody (Clone 7B1) 120111

$BLTR_1$, LTB_4 Receptor 1

Summary: Antigen: HeLa cells transfected with human BLT_1 • Host: mouse, clone 7B1 • Cross Reactivity: (+) human BLT_1 receptor; (-) BLT_2, $CysLT_1$, and $CysLT_2$ receptors • Application(s): FC, ICC, and IHC (frozen sections) • The human BLT_1 receptor is a GPCR that mediates the proinflammatory effects of LTB_4. Northern blotting reveals that the BLT_1 receptor is highly expressed in leukocytes, U937 cells, and to a much lower extent in spleen and thymus.

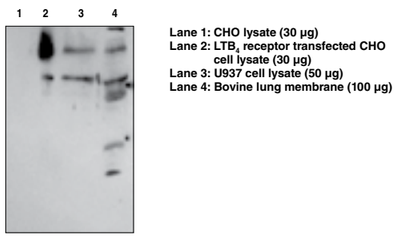
1 ea

BLT_1 Receptor Polyclonal Antibody 120114

$BLTR_1$, LTB_4 Receptor 1

Summary: Antigen: human BLT_1 receptor amino acids 331-352 • Host: rabbit • Cross Reactivity: (+) human and bovine BLT_1 receptor; (-) mouse BLT_1 receptor • Application(s): FC, ICC, IHC, and WB • The human BLT_1 receptor is a GPCR that mediates the proinflammatory effects of LTB_4. Northern blotting reveals that the BLT_1 receptor is highly expressed in leukocytes, U937 cells, and to a much lower extent in spleen and thymus.

1 ea



•Also Available: **BLT_1 Receptor Blocking Peptide** (120112)

BLT_1 Receptor Polyclonal Antiserum 100019

$BLTR_1$, LTB_4 Receptor 1

Summary: Antigen: human BLT_1 receptor amino acids 331-352 • Host: rabbit • Cross Reactivity: (+) human and bovine BLT_1 receptor; (-) mouse BLT_1 receptor • Application(s): confocal microscopy, FC, IHC, and WB • The human BLT_1 receptor is a GPCR that mediates the proinflammatory effects of LTB_4. Northern blotting reveals that the BLT_1 receptor is highly expressed in leukocytes, U937 cells, and to a much lower extent in spleen and thymus.

1 ea

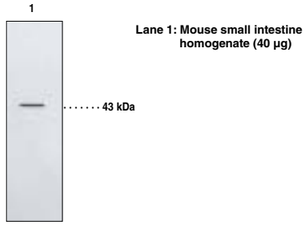
•Also Available: **BLT_1 Receptor Blocking Peptide** (120112)

BLT_2 Receptor Polyclonal Antibody 120124

$BLTR_2$, LTB_4 Receptor 2

Summary: Antigen: human BLT_2 receptor amino acids 325-338 • Host: rabbit • Cross Reactivity: (+) human and mouse BLT_2 receptor • Application(s): WB (recommended primarily for transfected cells) • The human BLT_2 receptor is a 358 amino acid GPCR with approximately 40% homology to BLT_1 at the amino acid level. The BLT_2 receptor is more broadly expressed than the BLT_1 receptor, with highest levels observed in liver, spleen, ovary, intestine, and peripheral blood leukocytes.

1 ea



•Also Available: **BLT_2 Receptor Blocking Peptide** (320124)

Bromoenol lactone 70700

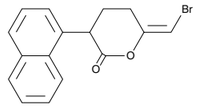
[88070-98-8] BEL, Haloenol lactone, HELSS

MF: $C_{16}H_{13}BrO_2$ **FW:** 317.2 **Purity:** ≥98%

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

Summary: A selective, irreversible, mechanism-based inhibitor of $iPLA_2$ (K_i = 60-180 nM)

5 mg
10 mg
25 mg
50 mg



•Also Available: **Bromoenol lactone-d_7** (9000528)
(R)-Bromoenol lactone (10006800)
(R)-Bromoenol lactone-d_7 (10534)
(S)-Bromoenol lactone (10006801)
(S)-Bromoenol lactone-d_7 (10535)

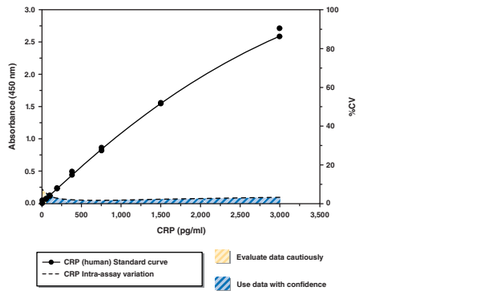
C-Reactive Protein (human) EIA Kit 10011236

CRP

Stability: ≥6 months at 4°C **Limit of Detection:** 46.9 pg/ml

Summary: CRP is a 224 amino acid protein that is synthesized primarily by hepatocytes, and to a lesser extent adipocytes. CRP plasma levels increase ~1,000-fold in response to acute and chronic inflammatory conditions, making it a useful gauge of inflammation in a wide range of physiological and pathological conditions. Cayman's CRP (human) EIA is a sensitive immunometric assay which can be used to measure CRP in plasma without prior sample purification.

96 wells



Caffeic Acid 70602

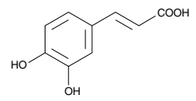
[331-39-5]

MF: $C_9H_8O_4$ **FW:** 180.2 **Purity:** ≥97%

A crystalline solid **Stability:** ≥2 years at room temperature

Summary: An inhibitor of 5-LO (IC_{50} = 3.7-72 µM) and 12-LO (IC_{50} = 5.1-30 µM)

5 g
10 g
25 g



Caffeic Acid phenylethyl ester 70750

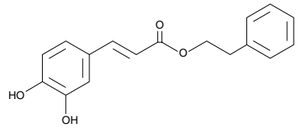
[104594-70-9] CAPE, 2-Phenylethyl Caffeate, β-Phenylethyl Caffeate

MF: $C_{17}H_{16}O_4$ **FW:** 284.3 **Purity:** ≥98%

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

Summary: A potent and specific inhibitor of NF-κB that exhibits antimitogenic, anticarcinogenic, anti-inflammatory, and immunomodulatory properties

50 mg
100 mg
500 mg
1 g



CAY10416 70635

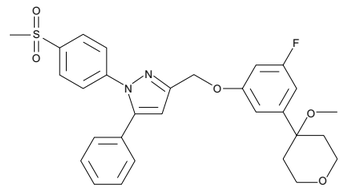
[443919-96-8]

MF: $C_{29}H_{29}FN_2O_5S$ **FW:** 536.6 **Purity:** ≥95%

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

Summary: A dual COX-2/5-LO inhibitor with IC_{50} values of 50 and 3 nM, respectively

1 mg
5 mg
10 mg
50 mg



CAY10471 10006735

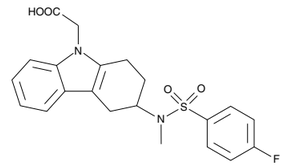
[627865-18-3]

MF: $C_{21}H_{21}FN_2O_4S$ **FW:** 416.5 **Purity:** ≥98%

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

Summary: An analog of BAY-u3405 which contains modifications that increase both its potency and selectivity for the human CRTH2/DP_2 receptor; binds to the human CRTH2/DP_2, DP_1, and TP receptors with K_i values of 0.6, 1200, and >10,000 nM, respectively

1 mg
5 mg
10 mg
50 mg



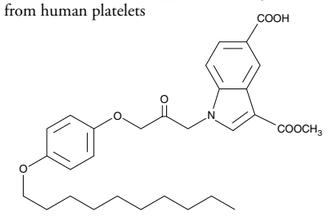
CAY10502 10008657

MF: $C_{30}H_{37}NO_7$ **FW:** 523.6 **Purity:** ≥98%

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

Summary: A potent inhibitor of $cPLA_{2\alpha}$ with an IC_{50} value of 4.3 nM for the purified enzyme from human platelets

500 µg
1 mg
5 mg
10 mg



CAY10512 10009536

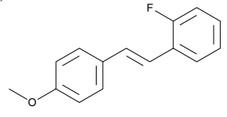
[139141-12-1]

MF: $C_{15}H_{13}FO$ **FW:** 228.3 **Purity:** ≥97%

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

Summary: A substituted *trans*-stilbene analog of resveratrol that is 100-fold more potent as measured by antioxidant activity; inhibits TNF-α-induced activation of NF-κB (IC_{50} = 0.15 µM)

10 mg
50 mg
100 mg
500 mg



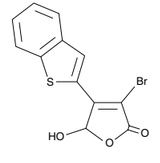
CAY10526 10010088

MF: $C_{12}H_7BrO_3S$ **FW:** 311.1 **Purity:** ≥98%

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

Summary: An inhibitor of mPGES-1 expression; inhibits PGE_2 production in LPS-stimulated RAW 264.7 cells (IC_{50} = 1.8 µM) without affecting COX-2 expression

1 mg
5 mg
10 mg
50 mg



CAY10571 10010400

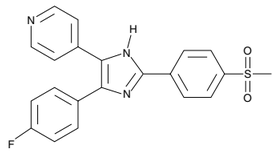
[152121-46-5]

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 SB 203580, 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



CAY10575 10011248

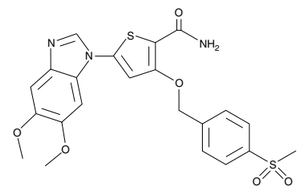
[916985-21-2]

MF: $C_{22}H_{21}N_3O_6S_2$ **FW:** 487.6 **Purity:** ≥95%

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

Summary: A benzimidazole analog that inhibits IKK-ε with an IC_{50} value of ~15.8 µM

1 mg
5 mg
10 mg
25 mg



CAY10576 10011249

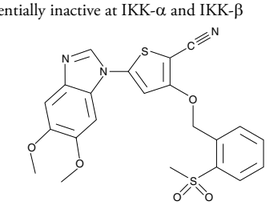
[862812-98-4]

MF: $C_{22}H_{19}N_3O_5S_2$ **FW:** 469.5 **Purity:** ≥95%

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

Summary: A benzimidazole analog that selectively inhibits IKK-ε with an IC_{50} value of 40 nM and is essentially inactive at IKK-α and IKK-β

1 mg
5 mg
10 mg
50 mg



CAY10589 13164

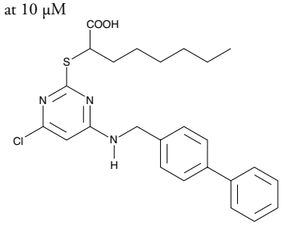
[1077626-52-8]

MF: $C_{25}H_{28}ClN_3O_2S$ **FW:** 470.0 **Purity:** ≥98%

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

Summary: A dual inhibitor of mPGES-1 (IC_{50} = 1.3 µM) and 5-LO (IC_{50} = 1.0 µM), inhibiting PGE_2 and LT synthesis in both cell free and intact cell assays; has minor effects on COX-1 and COX-2 activities, inhibiting these enzymes 34% and 38.8%, respectively, at 10 µM

1 mg
5 mg
10 mg
25 mg

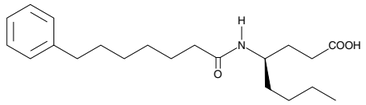


CAY10590 13181

[1101136-50-8]

MF: $C_{21}H_{33}NO_3$ **FW:** 347.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent and selective inhibitor of $sPLA_2$ that exhibits 95% inhibition ($X_I(50)$ = 0.003) of $sPLA_2$ without affecting the activities of $cPLA_2$ or $iPLA_2$

1 mg
5 mg
10 mg
50 mg

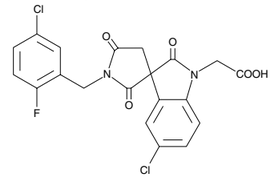


CAY10595 10012553

[916047-16-0]

MF: $C_{20}H_{13}Cl_2FN_2O_5$ **FW:** 451.2 **Purity:** ≥97%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent $CRTH2/DP_2$ receptor antagonist that binds to the human receptor with a K_i value of 10 nM; R-enantiomer of CAY10595 inhibits eosinophil chemotaxis induced by 13,14-dihydro-15-keto PGD_2 with an IC_{50} value of 7.3 nM

1 mg
5 mg
10 mg
50 mg

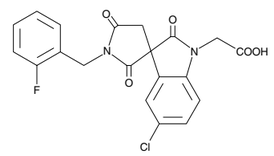


CAY10597 10012539

[916046-55-4]

MF: $C_{20}H_{14}ClFN_2O_5$ **FW:** 416.8 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent $CRTH2/DP_2$ receptor antagonist that binds to the human receptor with a K_i value of 37 nM; R-enantiomer of CAY10597 inhibits eosinophil chemotaxis induced by 13,14-dihydro-15-keto PGD_2 with an IC_{50} value of 40 nM

1 mg
5 mg
10 mg
50 mg

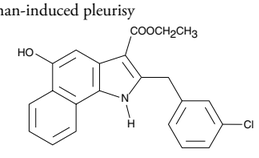


CAY10606 13381

[1159576-98-3]

MF: $C_{22}H_{18}ClNO_3$ **FW:** 379.8 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent, reversible inhibitor of 5-LO, in cell-free assays (IC_{50} = 86 nM), intact neutrophils (IC_{50} = 230 nM), and in whole blood (IC_{50} = 830 nM); significantly reduces both LT biosynthesis and inflammatory reaction in rats subjected to carrageenan-induced pleurisy

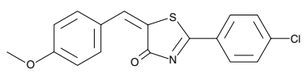
1 mg
5 mg
10 mg
25 mg



CAY10649 10804

MF: $C_{17}H_{12}ClNO_2S$ **FW:** 329.8 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A thiazolinone compound that directly inhibits 5-LO product formation in intact polymorphonuclear leukocytes and a soluble fraction of an S100 PMNL cell lysate (IC_{50}s = 0.28 and 0.09 µM, respectively)

1 mg
5 mg
10 mg
50 mg

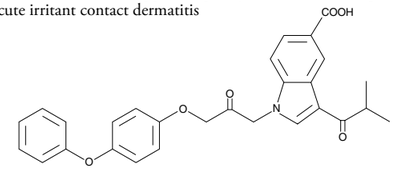


CAY10650 10743

CAS 1233706-88-1

MF: $C_{28}H_{25}NO_6$ **FW:** 471.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A highly potent (IC_{50} = 12 nM) $cPLA_{2\alpha}$ inhibitor; demonstrates strong anti-inflammatory effects when applied topically at a dose of 0.1 mg/ear in a murine model of acute irritant contact dermatitis

1 mg
5 mg
10 mg
50 mg

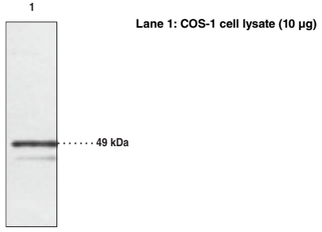


Chemokine-Like Receptor 1 Polyclonal Antibody 10325

ChemR23, CMKLR1, DEZ, GPCR ChemR23, Resolvin E1 Receptor

Peptide affinity-purified **Stability:** ≥ 1 year at -20°C
Summary: Antigen: human CMKLR1 amino acids 358–371 • Host: rabbit • Cross Reactivity: (+) human, mouse, rat, and monkey CMKLR1 • Application(s): FC, ICC, and WB • CMKLR1 is a GPCR relevant to the cellular chemotaxis of dendritic cells and macrophages. This receptor is also expressed in brain, liver, lung, and kidney tissues. Chemerin, or TIG2, has been identified as the natural ligand for this receptor. Resolvin E1 has also been identified as a ligand for CMKLR1; acting to dampen cellular responses to inflammation.

500 µl



• Also Available: **Chemokine-Like Receptor 1 Blocking Peptide** (10326)

COX Inhibitor Pack 10186

Purity: ≥98% **Stability:** ≥1 year at -20°C
Summary: Contains a combination of frequently used COX inhibitors; each kit contains aspirin, NS-398, CAY10404, SC-560, valeroyl salicylate, and resveratrol

1 ea

COX-1 (ovine) 60100

PG Endoperoxide Synthase, PGH Synthase 1

MF: Homodimer $\mathbf{M_r}$: 70 kDa/subunit **Purity:** ≥95%
Supplied in: 80 mM Tris-HCl, pH 8.0, containing 0.1% polysorbate and 300 µM DDC
Summary: Isolated from ram seminal vesicles • Specific activity: > 40,000 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.

5 Kunit
10 Kunit
50 Kunit

COX-2 (human recombinant) 60122

PGH Synthase 2

MF: Homodimer $\mathbf{M_r}$: 70 kDa **Purity:** ≥70%
Supplied in: 80 mM Tris-HCl, pH 8.0, with 0.1% polysorbate and 300 µM DDC
Summary: Recombinant N-terminal hexahistidine-tagged enzyme isolated from a *Baculovirus* overexpression system in Sf21 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 Kunit
2.5 Kunit
5 Kunit

COX Inhibitors

Product Name (Item No.)	COX-1 IC_{50} (µM)	COX-1 K_i (µM)	COX-2 IC_{50} (µM)	COX-2 K_i (µM)
COX-1 Selective				
FR122047 (10039)	0.028 (human)		65 (human)	
Phenylbutazone (70400)	16.0 (human)		>100 (human)	
Resveratrol (70675)	15.0 (ovine)	26.0 (ovine)		
SC-560 (70340)	0.009 (human)		6.3 (human)	
Valeroyl Salicylate (70670)	800 (ovine)		15,000 (ovine)	
COX-2 Selective				
CAY10404 (70210)	>500 (ovine)		<0.001 (ovine)	
DuP-697 (70645)	9.0 (human)		0.04 (human)	
Indomethacin heptyl ester (70271)	>66.0 (ovine)		0.04 (human)	
Indomethacin N-octyl amide (70273)	66.0 (ovine)		0.04 (human)	
N-(2-phenylethyl)-Indomethacin amide (70272)	50.0 (ovine)		0.125 (ovine) 0.06 (human)	
N-(3-pyridyl)-Indomethacin amide (70274)	75.0 (ovine)		50.0 (ovine) 0.052 (human)	
N-(4-acetamidophenyl)-Indomethacin amide (70278)	50.0 (ovine)		0.625 (ovine) 0.12 (human)	
Niflumic Acid (70650)	16.0 (human)	2.0 (ovine)	0.1 (human)	0.02 (ovine)
Nimesulide (70640)	70.0 (human) 22.0 (ovine)		1.27 (human) 0.03 (ovine)	
NS-398 (70590)	75.0 (human) 220 (ovine)		1.77 (human) 0.15 (ovine)	
SC-58125 (70655)	70 (cultured HUVEC cells)			
Non-Selective				
O-Acetyl Salicylhydroxamic Acid (70263)	4.5 mM (ovine)			
5-Aminosalicylic Acid (70265)	410 (human)		61.0 (human)	
Aspirin (70260)	750 (ovine)		1,250 (human)	
N-acetyl-2-carboxy Benzenesulfonamide (10008284)	0.06 (*in vitro*)		0.25 (*in vitro*)	
Diclofenac (sodium salt) (70680)	0.9 (human) 0.06 (ovine)		1.5 (human) 0.22 (ovine)	
(±)-Flurbiprofen (70250)	0.04 (human)		0.51 (human)	
Indomethacin (70270)	1.67 (human) 0.1 (ovine)		24.6 (human) 6.0 (ovine)	
(±)-Ibuprofen (70280)	2.6 (human)	9.0 (ovine)	1.53 (human)	9.0 (ovine)
Ketoprofen (10006661)	0.5 (human)		2.33 (human)	
Ketorolac (70690)	31.5 (human)		60.5 (human)	
Meclofenamate (sodium salt) (70550)	1.5 (human)		9.7 (human)	
6-methoxy Naphthalene Acetic Acid (70620)	20 (human)	21 (ovine)	20 (human)	19 (ovine)
(S)-Naproxen (70290)	0.6 (human)		2.0 (human)	
9,12-Octadecadiynoic Acid (90400)		0.6 (ovine)		
Peroxicam (13368)	1.57 (human)		1.69 (human)	
Sulindac (10004386)				

COX-2 (ovine) 60120

PG Endoperoxide Synthase, PGH Synthase 1
MF: Homodimer M_r: 70 kDa/subunit **Purity:** ≥95%
Supplied in: 80 mM Tris-HCl, pH 8.0, containing 0.1% polysorbate and 300 µM DDC
Summary: Isolated from ram seminal vesicles • Specific activity: >40,000 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.

5 Kunit
10 Kunit
50 Kunit

COX Inhibitor Screening Assays

Kit	Detection Method	Activity Measured	Format/ Time
COX (ovine) Inhibitor Screening Assay Kit (560101)	PGs generated in COX reaction are quantified by EIA	COX and peroxidase activities of ovine COX-1 and ovine COX-2	Generate PGs in COX reaction, then perform EIA
COX Inhibitor Screening Assay Kit (560131)	PGs generated in COX reaction are quantified by EIA	COX and peroxidase activities of ovine COX-1 and human recombinant COX-2	Generate PGs in COX reaction, then perform EIA
Colorimetric COX (ovine) Inhibitor Screening Assay Kit (760111)	Peroxidase activity is assayed colorimetrically by monitoring the appearance of oxidized TMPD	Peroxidase activity	Reactions performed in 96-well plate (answer in 30 minutes)
COX Fluorescent Inhibitor Screening Assay Kit (700100)	Fluorescence-based method for screening COX-1 and COX-2 isozyme-specific inhibitors	Peroxidase activity of ovine COX-1 and human recombinant COX-2	Reactions performed in 96-well plate (answer in 30 minutes)

Cayman Chemical's Inhibitor Screening Assays are used to screen for isozyme-specific inhibitors. All kits contain both COX-1 and COX-2

COX Activity Assays

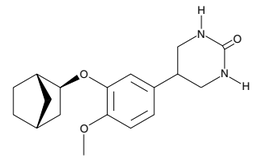
Kit	Detection Method	Activity Measured	Format
COX Activity Assay Kit (760151)	Colorimetric – monitors the appearance of oxidized TMPD	Peroxidase activity	96-well plate
COX Fluorescent Activity Assay Kit (700200)	Fluorometric – monitors the conversion of ADHP to resorufin Both assays include COX-1 and COX-2 specifc inhibitors in order to distinguish between the two enzymes	Peroxidase activity	96-well plate

Cayman Chemical's COX Activity Assay can be used to detect COX activity in cell lysates, tissue homogenates, and purified enzyme preparations.

CP 80633 13183

[135637-46-6]
MF: $C_{18}H_{24}N_2O_3$ **FW:** 316.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A selective inhibitor of phosphodiesterase 4 (PDE_4) (IC_{50} = 1.27 µM for PDE_4 *versus* >100 µM for PDE_1, PDE_2, PDE_3, and PDE_5); inhibits eosinophil superoxide production (IC_{50} <0.6 µM) and blocks LPS-induced TNF-α release from monocytes (IC_{50} = 0.22 µM); significantly reduces antigen-induced airway inflammation in atopic guinea pigs, monkeys, and mice.

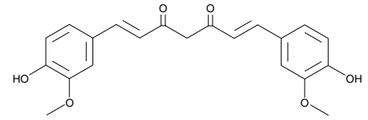
500 µg
1 mg
5 mg
10 mg



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, anti-tumor and anti-inflammatory properties

1 g
5 g
10 g
50 g

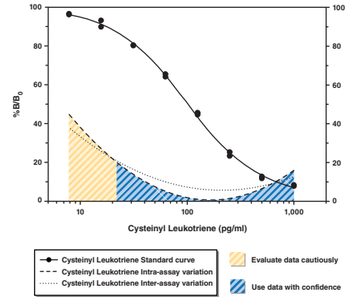


•Also Available: **Curcumin (technical grade)** (81025.1)

Cysteinyl Leukotriene EIA Kit 500390

Stability: ≥6 months at -80°C
Sensitivity: 50% B/B_0: 103 pg/ml • 80% B/B_0: 34 pg/ml
Summary: LTs are a group of acute inflammatory mediators derived from arachidonic acid *via* the 5-LO pathway in leukocytes. LTC_4, LTD_4, and LTE_4 are collectively referred to as CysLTs. LTC_4 and LTD_4 are potent mediators of asthma and hypersensitivity. They induce bronchoconstriction, increase microvascular permeability, and are vasoconstrictors of coronary arteries. The biological activity of LTE_4 is much lower in most systems studied, but its presence reflects the prior existence of LTC_4 and LTD_4. Cayman's CysLT EIA Kit is a competitive assay based on a proprietary high-affinity monoclonal antibody that can be used for quantification of CysLT in urine and other sample matrices.

96 strip/solid wells
480 strip/solid wells



•Also Available: **Cysteinyl Leukotriene Express EIA Kit** (10009291)
Luminex® Cysteinyl Leukotriene Kit (10007577)

Cyclooxygenase Antibodies

Antibody	Antigen	Cross Reactivity	Application	Supplied As
COX Polyclonal Antibody Item No. 160103	Purified ovine COX-1 **Host:** rabbit	Non-specific; reacts with both COX-1 and COX-2 (primarily COX-1)	WB - 1:1,000 IHC	500 µg IgG
COX-2 (mouse) Polyclonal Antibody Item No. 160106	Amino acids 570-598 from mouse COX -2 **Host:** rabbit	(+) ovine, human, mouse, rabbit, monkey, guinea pig, and rat COX-2 (-) COX-1 (all species)	WB - 1:1,000 IHC (frozen and paraffin-embedded tissue sections) - 1:100 - 1:1,000	Peptide affinity-purified IgG
COX-2 (human) Polyclonal Antibody Item No. 160107	Amino acids 567-599 from human COX-2 **Host:** rabbit	(+) ovine, human, mouse, guinea pig, and rat COX-2 (-) COX-1 (all species)	WB - 1:1,000 IHC (frozen and paraffin-embedded tissue sections) - 1:100 - 1:1,000	Peptide affinity-purified IgG
COX-1 (ovine) Polyclonal Antiserum Item No. 160108	Amino acids 272-282 from ovine COX-1 **Host:** rabbit	(+) ovine, human, and bovine COX-1 (-) rat and mouse COX-1 (-) ovine, human, and mouse COX-2	WB - 1:1,000 IHC ICC	200 µl lyopholized antiserum
COX-1 (mouse) Polyclonal Antibody Item No. 160109	Amino acids 274-288 from mouse COX-1 **Host:** rabbit	(+) mouse and rat COX-1 (-) human and ovine COX-1 (-) mouse, rat, human, and ovine COX-2	WB - 1-2 µg/ml IHC - This antibody is particularly well suited for IHC (paraffin-embedded mouse tissues) 2-5 µg/ml	Peptide affinity-purified IgG
COX-1 Monoclonal Antibody Item No. 160110	Purified ovine COX-1 **Host:** mouse	(+) ovine, bovine, human, mouse, and rat COX-1, ovine COX-2 (50%), human COX-2 (5%) (-) mouse COX-2	WB - 5 µg/ml IHC (frozen and paraffin-embedded tissue sections) - 10-20 µg/ml	500 µg lyophilized IgG_{2b}
COX-1 Monoclonal FITC Antibody Item No. 160111	Purified ovine COX-1 **Host:** mouse	(+) ovine, bovine, human, mouse, and rat COX-1, ovine COX-2 (50%), human COX-2 (5%) (-) mouse COX-2	FC - This product is derived by labeling the COX-1 monoclonal antibody (item no. 160110) with fluorescein. No secondary antibody is required for detection.	250 µg IgG_{2b}
COX-2 Monoclonal Antibody Item No. 160112	Amino acids 580-599 from human COX-2 **Host:** mouse	(+) human, monkey, and ovine COX-2 (-) mouse, rat, and rabbit COX-2 and COX-1 (all species)	WB - 0.5 µg/ml IHC (frozen and paraffin-embedded tissue sections) - 1-2 µg/ml	50 µg lyophilized IgG_1
COX-2 Monoclonal FITC Antibody Item No. 160113	Amino acids 580-599 from human COX-2 **Host:** mouse	(+) human, monkey, and ovine COX-2 (-) mouse, rat, and rabbit COX-2 and COX-1 (all species)	FC - This product is derived by labeling the COX-2 monoclonal antibody (item no. 160112) with fluorescein. No secondary antibody is required for detection.	100 µg IgG_1
COX-2 (mouse) Polyclonal Antiserum Item No. 160116	Amino acids 584-598 from mouse COX-2 **Host:** rabbit	(+) mouse, rat, ovine, human, rabbit, monkey, and guinea pig COX-2 (-) COX-1 (all species)	WB - 1:1,000 IHC (frozen and paraffin-embedded tissue sections)	50 µl lyophilized antiserum
COX-1 Monoclonal PE Antibody Item No. 160120	Purified ovine COX-1 **Host:** mouse	(+) human, ovine, bovine, rat, and mouse COX-1, ovine COX-2 (50%) and human COX-2 (5%) (-) mouse COX-2	FC - This product is derived by labeling the COX-1 monoclonal antibody (item no. 160110) with phycoerythrin. No secondary antibody is required for detection.	Purified IgG_{2b} in PBS containing 0.1% sodium azide and 4 mg/ml BSA
COX-2 Monoclonal PE Antibody Item No. 160122	Amino acids 580-599 from human COX-2 **Host:** mouse	(+) human, monkey, and ovine COX-2 (-) mouse, rat, and rabbit COX-2 and COX-1 (all species)	FC - This product is derived by labeling the COX-2 monoclonal antibody (item no. 160112) with phycoerythrin. No secondary antibody is required for detection.	Purified IgG_{2b} in PBS containing 0.1% sodium azide and 4 mg/ml BSA
COX-2 (mouse) Polyclonal Antibody (Affinity-Purified) Item No. 160126	Amino acids 584-598 from mouse COX-2 **Host:** rabbit	(+) mouse, rat, ovine, and human COX-2; other species not tested (-) COX-1 (all species)	WB - 1 µg/ml IHC - 1-2.5 µg/ml This antibody is particularly well suited for IHC (frozen and paraffin-embedded tissue sections).	Peptide affinity-purified IgG
Goat Anti-COX-2 (human) Polyclonal Antibody (Affinity-Purified) Item No. 100034	Amino acids 578-596 from human COX-2 **Host:** goat	(+) human, COX-2; other species not tested (-) COX-1 (all species)	WB ICC IHC (formalin-fixed paraffin-embedded sections)	Peptide affinity-purified IgG
COX-2 (mouse) Polyclonal FITC Antibody Item No. 10010096 CAYMAN EXCLUSIVE	Amino acids 570-598 from mouse COX-2 **Host:** rabbit	(+) mouse, rat, and human COX-2 (-) COX-1 (all species)	FC ICC WB	Peptide affinity-purified IgG-fluorescein

vol. 13 In

Thomas G. Brock, Ph.D.

Lipoxins and Resolvins

In life, each beginning anticipates an ending. Day becomes night, spring gives way to autumn, and birth must inevitably lead to death. Within the body, an injury should be followed by a process of healing. If the skin is broken, steps are triggered to, first, limit the damage and, second, repair the rupture. If the cut skin becomes infected, then inflammation will begin, but this must end, too. We now know that lipoxins and resolvins are natural compounds that initiate the ending of inflammation. Perhaps more importantly, these biomolecules, or their analogs, can be applied to inflammatory sites to quell both acute and intractable, chronic inflammation. This article looks at how lipoxins and resolvins are made in the body and how they impact various inflammatory diseases.

Lipoxins

What happens when you get a number of different activists with their own agendas together? While this could pose serious problems for human activists, activated cells at a site of infection work together to produce lipoxins. Lipoxins (LX) are trihydroxy products derived from arachidonic acid (AA) through the cooperative interaction of neighboring cells. In the healthy body, these cells do not usually gather together and do not release large amounts of AA. However, in the inflammatory milieu, neutrophils, eosinophils, monocytes, platelets, and endothelial cells are found packed together, abutting one another as they join forces to fight inflammation. During the early hours of infection, these cells unleash an assortment of bioactive chemicals, including gelatinases, myeloperoxidase, reactive oxygen and nitrogen species, eicosanoids, and cytokines. In addition to directly attacking invaders, this arsenal facilitates an orchestrated response, recruiting additional immune cells, promoting vascular leak, and preventing clot formation. Following a successful defense, the battle area must be cleared of debris, defending immune cells eliminated, and damaged tissues repaired. In the late stages of the defense against infection, different cells cooperate to produce two LX species for the purpose of initiating these changes.

The dense clustering of different cell types during inflammation presents a unique situation for lipid handling. In contrast to the synthesis of protein mediators (*e.g.*, cytokines), lipid mediators can be produced along enzyme pathways that involve multiple cells, in a process known as transcellular biosynthesis. A well-documented example concerns the substrate, AA. This polyunsaturated fatty acid is normally stored in membrane phospholipids. In response to diverse conditions that trigger a transient rise in cytoplasmic calcium levels, cytosolic phospholipase A_2 releases AA from perinuclear membranes.[1] Remarkably, much of this free AA is immediately secreted into the extracellular milieu, where it can be taken up and used by nearby cells; many different cell types can act as either donors or recipients.[2] In this way, AA metabolism at the site of inflammation is determined more by the integrated enzymatic actions of the diverse types of cells that are present. In essence, the inflamed tissue becomes a specialized organ for lipid metabolism, producing the types and amounts of lipid mediators needed to promote or resolve inflammation.

There are two major routes of LX production from AA in humans. These can be distinguished by the type of lipoxygenase which initiates AA oxygenation, and these are distributed differently by cell type (Figure 1). The first pathway involves the insertion of molecular oxygen at C-5 by 5-lipoxygenase (5-LO) in concert with the 5-LO activating protein (FLAP) to produce 5-hydroperoxyeicosatetraenoic acid (5-HpETE), which is further metabolized by 5-LO to produce the intermediate, leukotriene A_4 (LTA_4). This pathway is conducted solely by leukocytes, since the distribution of 5-LO is largely restricted to these cell types. LTA_4 is readily transferred to adjacent cells, usually leading to its processing to other LTs.[3] However, adherent platelets, *via* 12-LO, will convert LTA_4, donated by leukocytes, to LXA_4 and LXB_4.[4,5] The second major route of LX biosynthesis involves the initial conversion of AA to 15(S)-HpETE by 15-LO. This enzyme is abundant in epithelial cells lining the respiratory or gastrointestinal tracts, as well as in diverse leukocytes, including eosinophils, monocytes, and macrophages. Following secretion, 15(S)-HpETE is taken up by either neutrophils or monocytes and rapidly converted through a 5-LO/FLAP dependent mechanism to LXA_4 and LXB_4.[6,7] In addition, epimers of LXA_4 and LXB_4 can be produced following aspirin treatment. Aspirin irreversibly acetylates cyclooxygenase-2 (COX-2), inhibiting its ability to produce prostanoids. However, acetylated COX-2 can metabolize AA to 15(R)-HETE, which may then be processed to the "aspirin-triggered" LX by 5-LO.

There is abundant evidence that LX have anti-inflammatory effects, altering the actions of diverse cell types in a wide range of conditions. Many of these actions involve inhibition: stopping neutrophil chemotaxis and transmigration, preventing IL-8 production in enterocytes, blocking TNF-α secretion by lymphocytes, and eliminating reactive oxygen species from endothelial cells. However, LX also initiate positive anti-inflammatory effects, such as stimulating the phagocytosis of apoptotic cells by macrophages, increasing the formation of prostacyclin, which inhibits platelet aggregation, in endothelial cells, and up-regulating CCR5 expression in T cells. A more thorough list of cellular and physiological effects of LX may be obtained from recent reviews.[5,8] Cayman is your source for lipoxins (Table 1).

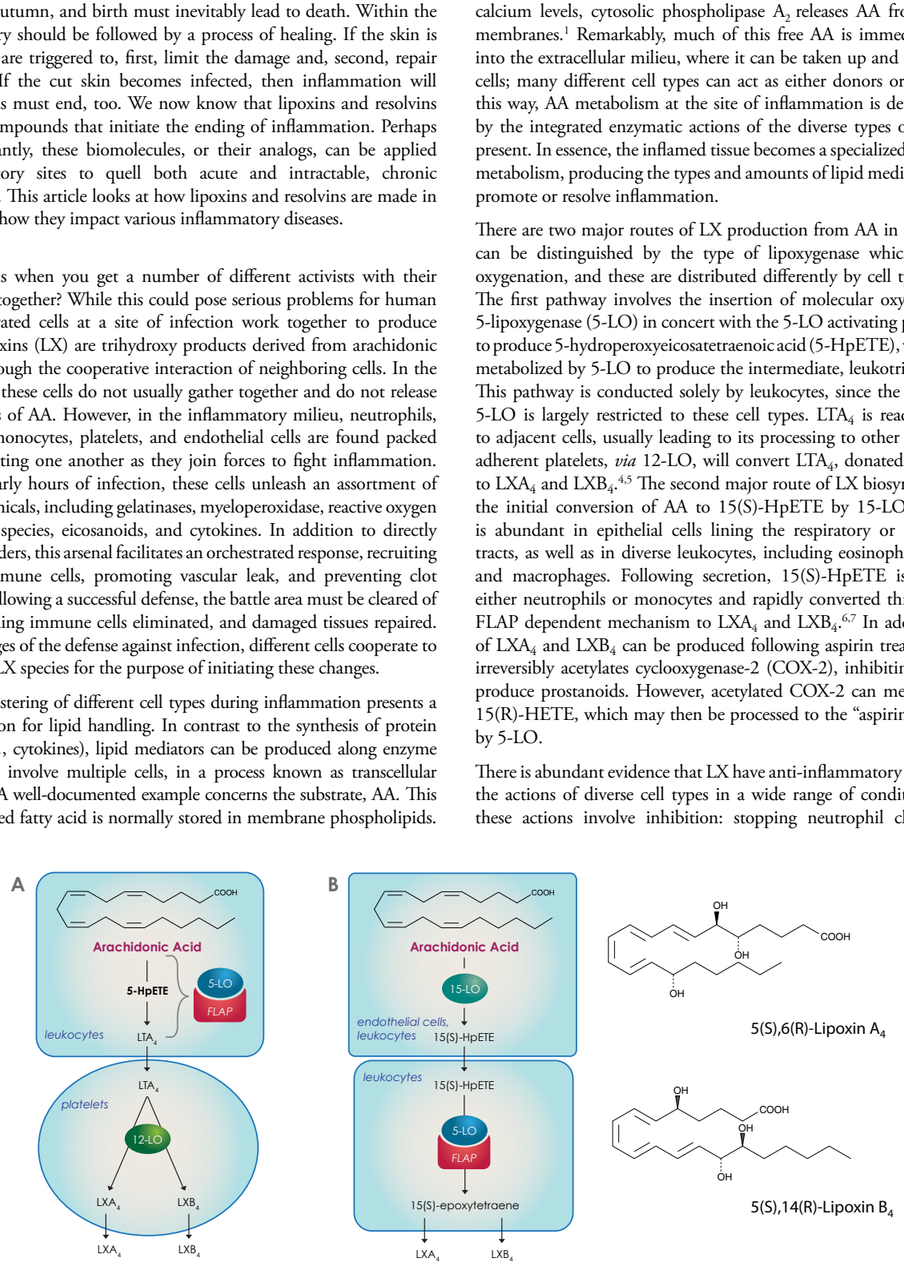


Figure 1. Lipoxin biosynthesis and structures. The synthesis of LXA_4 and LXB_4 involves (A) leukocyte-platelet or (B) endothelial cell/leukocyte-leukocyte cooperativity. (C). LXA_4 and LXB_4 are trihydroxy derivatives of AA.

Table 1. Lipoxins available from Cayman

Item No.	Product Name
10011453	Lipoxin A_5 *Exclusive*
90410	5(S),6(R)-Lipoxin A_4
10007737	5(S),6(R)-Lipoxin A_4-d_5 *Exclusive*
10033	5(S),6(R)-Lipoxin A_4 methyl ester
10049	5(S),6(S)-Lipoxin A_4
90415	5(S),6(R),15(R)-Lipoxin A_4
90420	5(S),14(R)-Lipoxin B_4

For a full product listing, please visit www.caymanchem.com

Resolvins

Resolvins (Rv) are endogenous chemical mediators that are biosynthesized from the major ω-3 fatty acids, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), denoted E series (RvE) and D series (RvD) resolvins, respectively. Like LX, Rv can be produced through transcellular cooperation, initiated by enzymes in epithelial cells and completed by adjacent leukocytes. Also like LX, aspirin-triggered Rv epimers are produced by the acetylated COX-2/5-LO pathway. Conceptually, the substrates EPA and DHA are released from membrane phospholipids, metabolized in a transcellular fashion, and secreted in amounts sufficient to reverse the course of inflammation. Ideally, this must happen throughout the inflamed tissue, at a time that appropriately follows the elimination of the insult which caused the inflammation, continuing on to a return to homeostasis. Presumably, the EPA-poor Western diet presents the possibility of failure to resolve inflammation, due to reduced capacity to produce RvE. On the other hand, tissues rich in DHA (*e.g.*, eye, brain, central nervous system) have a ready stock of substrate for RvD generation.

RvE1, perhaps the best-studied Rv, has multiple effects both on individual cells and on the inflammatory response *in vivo*. At nanomolar concentrations, RvE1 blocks LTB_4-stimulated actin polymerization and CD11b surface expression on human neutrophils. RvE1 inhibits neutrophil migration across endothelial and epithelial barriers, blocks the oxidative burst, down-regulates the expression of L-selectin and CD11b/CD18 to reduce neutrophil adhesion, and up-regulates the decoy receptor CCR5 on apoptotic neutrophils. In macrophages, RvE1 greatly increases the phagocytosis of apoptotic neutrophils and thymocytes as it specifically drives phenotypic switching from the classically activated (M1) macrophage to a resolution-phase (rM) cell type. The rM phenotype differs from the M1 by expression of the mannose receptor Ym-1, the enzyme arginase-1, and the anti-inflammatory cytokine IL-10. In inflamed corneas, RvE1 decreases the production of TNF-α and IL-1 (α and β) while blocking neovascularization by suppressing VEGF generation. Notably, administered LX and Rv are effective at preventing, slowing, stopping, or reversing inflammation in many mouse models of disease, even though lipid mediators are notoriously short-lived. Additional actions of Rv may be found in recent reviews.[9,10] Cayman has select Rv compounds and DHA derivatives available (Table 2).

Table 2. Resolvins and DHA derivatives available from Cayman

Item No.	Product Name
10008128	10(S),17(S)-DiHDoHE *Exclusive*
10005099	17(R)-HDoHE *Exclusive*
10009799	17(S)-HDoHE
13185	17(S)-HpDoHE
10012554	Resolvin D1 *Exclusive*
13060	17(R)-Resolvin D1 *Exclusive*
10007279	Resolvin D2 *Exclusive*

For a full product listing, please visit www.caymanchem.com

Moving To Market

There remain significant challenges to understanding if, when, and how LX and Rv naturally act during inflammatory events. However, there is overwhelming evidence that certain of these lipid mediators have profound physiological effects. The challenge then becomes developing stable analogs, formulations, and routes of delivery that efficiently and effectively treat disease. Berlex Biosciences (now part of Bayer HealthCare) is one company that has taken on this challenge, introducing several stable LX analogs for intravenous, oral, and topical administration.[11] Two compounds, ZK-142 and ZK-994, demonstrated broad anti-inflammatory effectiveness in a variety of models. In additional studies, ZK-994 reduced many measurements of airway inflammation in mouse models of allergic response.[12]

Resolvyx Pharmaceuticals is developing Rv therapeutics. Started in 2005, they have developed RX-10045, a synthetic resolvin, and are also testing two natural lipids, RvE1 (named RX-10001) and neuroprotectin (RX-20001), a natural DHA derivative (Figure 2). RX-10045 has passed a Phase II clinical trial for treating chronic dry eye syndrome. Dry eye syndrome is one of the most common problems treated by ophthalmologists (with a $1.7 billion global market) that can have many different causes and outcomes. Certain tear-deficient forms are characterized by chronic inflammatory infiltration of the lacrimal and salivary glands with $CD4^+$ T cells.[13] In a mouse model of dry eye syndrome, either RvE1 or a methyl ester prodrug of RvE1 was effective at reducing inflammation, including the number of $CD4^+$ cells in cornea.[14] Possibly, you can expect to find eyedrops containing RvE1 or an RvE1 analog in the near future.

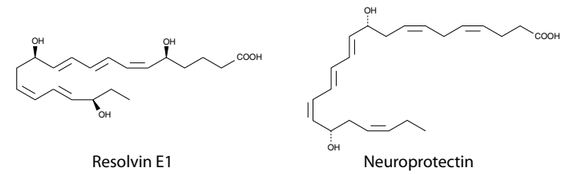


Figure 2. Structures of RvE1 and neuroprotectin. Neuroprotectin is a dihydroxy derivative of DHA.

References

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β-Defensin-2 (human recombinant) 10011217

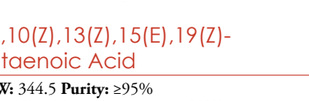
Antimicrobial Peptide, hBD-2
M_r: 4.6 kDa **Purity:** ≥90%
Supplied in: 50 mM Tris HCl, pH 8.0, containing 500 mM sodium chloride and 20% glycerol
Summary: Recombinant protein expressed in *E. coli* • Expression is regulated in response to infection and inflammation; links innate and adaptive immunity by attracting immature dendritic cells and memory T-cells; has antimicrobial, antiviral, and immunomodulatory properties which increase resistance to infection

5 µg
10 µg
25 µg

5(S),6(R)-DiHETE 35200

[82948-88-7]
MF: $C_{20}H_{32}O_4$ **FW:** 336.5 **Purity:** ≥98%
A solution in ethanol **Stability:** ≥1 year at -20°C
Summary: A dihydroxy PUFA and a nonenzymatic hydrolysis product of LTA_4

25 µg
50 µg
100 µg
250 µg

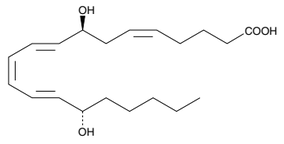


• Also Available: **5(S),6(R)-DiHETE Lipid Maps MS Standard** (10007252)

8(S),15(S)-DiHETE 35370

[80234-65-7]
MF: $C_{20}H_{32}O_4$ **FW:** 336.5 **Purity:** ≥98%
A solution in ethanol **Stability:** ≥1 year at -20°C
Summary: A product of arachidonic acid formed when 15(S)-HETE is subjected to further oxidation by 15-LO; causes eosinophil chemotaxis (ED_{50} = 1.5 µM)

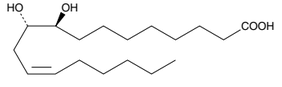
25 µg
50 µg
100 µg
250 µg



(±)9,10-DiHOME 53400

[263399-34-4] Leukotoxin diol
MF: $C_{18}H_{34}O_4$ **FW:** 314.5 **Purity:** ≥98%
A solution in methyl acetate **Stability:** ≥1 year at -20°C
Summary: Racemic version of a product of epoxide hydrolase metabolism of leukotoxin, the 9(10) epoxide of linoleic acid generated by neutrophils during the oxidative burst

25 µg
50 µg
100 µg
500 µg



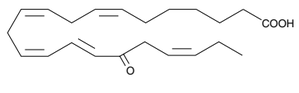
NOTE: relative stereochemistry shown in chemical structure

• Also Available: **(±)9,10-DiHOME-d_4** (10009993)

17-keto-7(Z),10(Z),13(Z),15(E),19(Z)-Docosapentaenoic Acid 9000347

MF: $C_{22}H_{32}O_3$ **FW:** 344.5 **Purity:** ≥95%
A solution in ethanol **Stability:** ≥6 months at -80°C
Summary: A metabolite of lipoxygenase-mediated oxidation of DPA; activates Nrf2-dependent antioxidant gene expression, acts as a PPARγ agonist (EC_{50} ~200 nM), and inhibits pro-inflammatory cytokine and nitric oxide production at biological concentration ranges (5-25 µM)

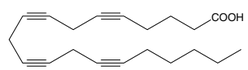
100 µg
250 µg
500 µg
1 mg



Eicosatetraynoic Acid 90120

[1191-85-1] ETYA
MF: $C_{20}H_{24}O_2$ **FW:** 296.4 **Purity:** ≥98%
White orthorhombic flakes **Stability:** ≥1 year at -20°C
Summary: A nonspecific inhibitor of COXs and LOs; inhibits human platelet 12-LO and COX-1 with IC_{50} values of 4 and 8 µM, respectively

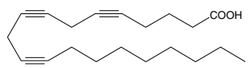
5 mg
10 mg
25 mg
50 mg



5,8,11-Eicosatriynoic Acid 90200

[13488-22-7] 5,8,11-ETI
MF: $C_{20}H_{28}O_2$ **FW:** 300.4 **Purity:** ≥99%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A nonselective LO inhibitor; inhibits A23187 and L-cysteine induced LTC_4 biosynthesis in murine mastocytoma cells; also inhibits COX

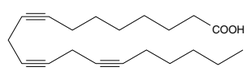
1 mg
5 mg
10 mg
50 mg



8,11,14-Eicosatriynoic Acid 10007900

[13488-22-7] 8,11,14-ETI
MF: $C_{20}H_{28}O_2$ **FW:** 300.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An inhibitor of COX (IC_{50} = 14 µM), human 12-LO (IC_{50} = 0.46 µM), 5-LO (IC_{50} = 25 µM), and the actions of SRS-A (IC_{50} = 10 µM)

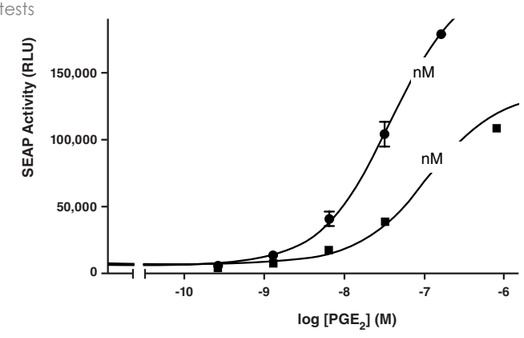
1 mg
5 mg
10 mg
50 mg



EP_2 Receptor (rat) STEP Reporter Assay Kit (Luminescence) 600340

PGE_2 Receptor 2
Stability: ≥1 year at -20°C
Summary: The EP_2 receptor is one of four GPCRs that mediate the actions of PGE_2. The diverse effects of PGE_2 acting *via* EP_2 receptors point to the need to identify novel agonists and antagonists, both to further elucidate the function of this receptor subtype and for use as therapeutics for various diseases. Cayman's EP_2 Receptor (rat) STEP Reporter Assay Kit (Luminescence) consists of a 96-well plate coated with both rat EP_2 receptor and Secreted Alkaline Phosphatase (SEAP) reporter constructs (EP_2 Receptor STEP Plate). Cells grown on the STEP complex will express EP_2 at the cell surface. Binding of agonists to EP_2 initiates a signal transduction cascade resulting in expression of SEAP which is secreted into the cell culture media. Aliquots of media are removed at time intervals, beginning at approximately six hours, and SEAP activity is measured following addition of a luminescence-based alkaline phosphatase substrate provided in the kit. The kit is simple to use and can be easily adapted to high throughput screening for therapeutic compounds regulating the activation of EP_2.

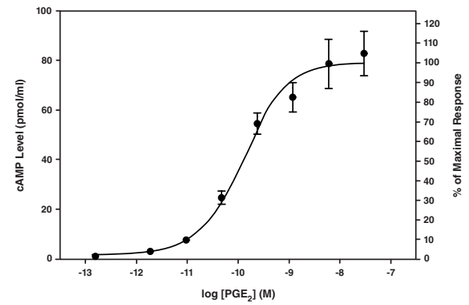
100 tests



EP_4 Receptor (rat) STEP Plate Assay Kit (cAMP method) 600410

PGE_2 Receptor 4
Stability: ≥1 year at -20°C
Summary: Cayman's EP_4 Receptor (rat) STEP Plate Assay Kit (cAMP method) consists of a 96-well plate coated with a proprietary STEP transfection complex containing EP_4 constructs and an optimized mixture of native and recombinant proteins (EP_4 STEP Strip Plate). Cells grown on the STEP complex will express EP_4 at the cell surface. Binding of agonists to EP_4 stimulates cAMP generation and increases intracellular cAMP levels, which can be measured by a competitive EIA using the reagents included in the kit.

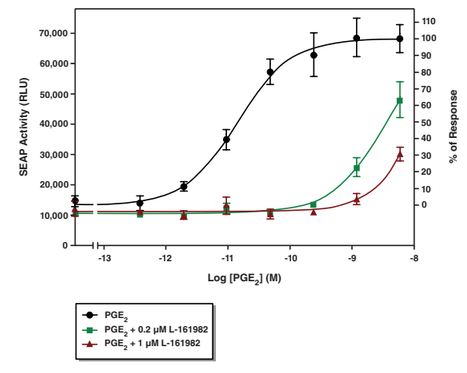
1 ea



EP_4 Receptor (rat) STEP Reporter Assay Kit (Luminescence) 600350

PGE_2 Receptor 4
Stability: ≥1 year at -20°C
Summary: Cayman's EP_4 Receptor (rat) STEP Reporter Assay Kit (Luminescence) consists of a 96-well plate coated with both rat EP_4 receptor and Secreted Alkaline Phosphatase (SEAP) reporter constructs (EP_4 Receptor STEP Plate). Cells grown on the STEP complex will express EP_4 at the cell surface. Binding of agonists to EP_4 initiates a signal transduction cascade resulting in expression of SEAP which is secreted into the cell culture media. Aliquots of media are removed at time intervals, beginning at approximately six hours, and SEAP activity is measured following addition of a luminescence-based alkaline phosphatase substrate provided in the kit. The kit is simple to use and can be easily adapted to high throughput screening for therapeutic compounds regulating the activation of EP_4.

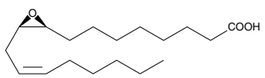
100 tests



(±)9(10)-EpOME 52400

9,10-EODE, Leukotoxin
MF: $C_{18}H_{32}O_3$ **FW:** 296.5 **Purity:** ≥98%
A solution in methyl acetate **Stability:** ≥2 years at -20°C
Summary: Racemic version of the 9,10-epoxide of linoleic acid generated by neutrophils during the oxidative burst

25 µg
50 µg
100 µg
250 µg



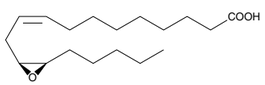
NOTE: relative stereochemistry shown in chemical structure

• Also Available: **(±)9(10)-EpOME-d_4** (10009995)

(±)12(13)-EpOME 52450

12,13-EODE, iso-Leukotoxin
MF: $C_{18}H_{32}O_3$ **FW:** 296.5 **Purity:** ≥98%
A solution in methyl acetate **Stability:** ≥1 year at -20°C
Summary: Racemic version of the 12,13-*cis* epoxide of linoleic acid generated by neutrophils during the oxidative burst

25 µg
50 µg
100 µg
250 µg



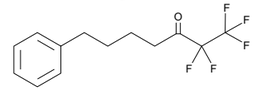
NOTE: relative stereochemistry shown in chemical structure

• Also Available: **(±)12(13)-EpOME-d_4** (10009996)

FKGK 11 13179

[1071000-98-0]
MF: $C_{13}H_{13}F_5O$ **FW:** 280.2 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A selective inhibitor of $iPLA_2$ that demonstrates an $X_i(50)$ value of 0.0073; in comparison, mole fractions as high as 0.091 do not inhibit $cPLA_2$ activity and cause only slight inhibition of $sPLA_2$

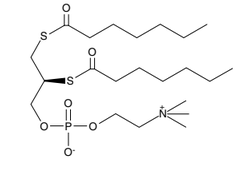
500 µg
1 mg
5 mg
10 mg



1,2-*bis*(heptanoylthio) Glycerophosphocholine 62235

[89019-63-6] Diheptanoyl Thio-PC, 1,2-bis(Heptanoylthio)-1,2-dideoxy-sn-glycero-3-phosphorylcholine
MF: $C_{22}H_{44}NO_6PS_2$ **FW:** 513.7 **Purity:** ≥95%
A solution in ethanol **Stability:** ≥1 year at -20°C
Summary: A colorimetric substrate for all PLA_2s with the exception of $cPLA_2$ and PAF-AH

5 mg
10 mg
25 mg
50 mg



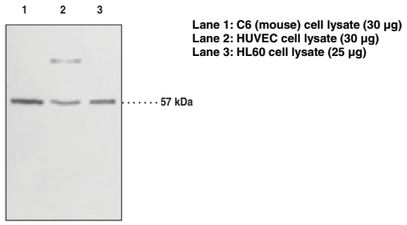
GPR17 (C-Term) Polyclonal Antibody 10136

G protein-coupled receptor 17

Peptide affinity-purified **Stability:** ≥ 1 year at -20°C

Summary: Antigen: human GPR17 amino acids 351-367 • Host: rabbit • Cross Reactivity: (+) human, mouse, and rat GPR17 • Application(s): FC, ICC, and WB • GPR17 is a GPCR that has been identified as a dualistic receptor recognizing signals from two unrelated chemical families: nucleotides and CysLTs.The deorphanization of GPR17 supports the suggested crosstalk between nucleotides and CysLTs during inflammation and injury.

500 µl



Lane 1: C6 (mouse) cell lysate (30 µg)
Lane 2: HUVEC cell lysate (30 µg)
Lane 3: HL60 cell lysate (25 µg)

GW 627368X 10009162

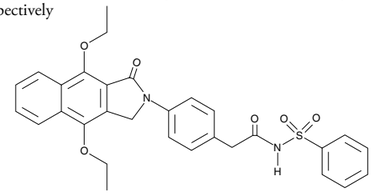
[439288-66-1]

MF: $C_{30}H_{28}N_2O_6S$ **FW:** 544.6 **Purity:** ≥96%

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

Summary: A potent and selective EP_4 receptor antagonist with additional human TP receptor affinity; binds to human EP_4 and TP receptors with K_i values of 100 and 158 nM, respectively

1 mg
5 mg
10 mg
25 mg



GW 848687X 10010410

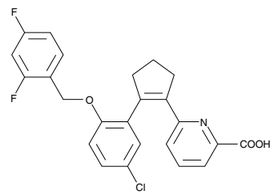
[612831-24-0]

MF: $C_{24}H_{18}ClF_2NO_3$ **FW:** 441.9 **Purity:** ≥98%

A solution in methyl acetate **Stability:** ≥1 year at -20°C

Summary: A potent and selective EP_1 receptor antagonist (IC_{50} = 2.5 nM) with > 400-fold selectivity relative to EP_2, EP_3, EP_4, DP_1, and IP; has 30-fold selectivity over TP; shows complete anti-hyperalgesic activity in a rat model of chronic inflammatory joint pain

500 µg
1 mg
5 mg
10 mg



GYY 4137 13345

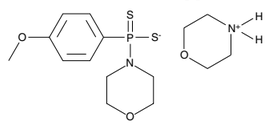
[106740-09-4]

MF: $C_{11}H_{16}NO_2PS_2 \bullet C_4H_{10}NO$ **FW:** 377.5 **Purity:** ≥95%

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

Summary: A water-soluble, slow-releasing H_2S donor which demonstrates vasodilator and anti-hypertensive activity in hypertensive rats when given intravenously; also protects against endotoxic shock in rats, inhibiting pro-inflammatory signaling

10 mg
25 mg
50 mg
100 mg



17(S)-HDoHE 10009799

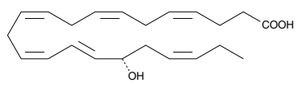
17(S)-hydroxy Docosahexaenoic Acid

MF: $C_{22}H_{32}O_3$ **FW:** 344.5 **Purity:** ≥98%

A solution in ethanol **Stability:** ≥2 years at -20°C

Summary: A primary mono-oxygenation product of DHA in human whole blood, human leukocytes, and murine brain and serves as a precursor to 17(S)-resolvins

25 µg
50 µg
100 µg
250 µg



HEPC 10006695

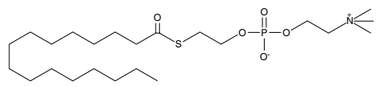
[60793-01-3] 2-Hexadecanoylthio-1-Ethylphosphorylcholine

MF: $C_{23}H_{48}NO_5PS$ **FW:** 481.7 **Purity:** ≥95%

A solution in ethanol **Stability:** ≥1 year at -20°C

Summary: A chromogenic substrate for Type II PLA_2 enzymes, such as porcine pancreatic, bee venom, and snake venom PLA_2

5 mg
10 mg
25 mg
50 mg



5(S),6(R)-7-trihydroxymethyl Heptanoate 10005032

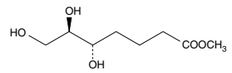
BML-111

MF: $C_8H_{16}O_5$ **FW:** 192.2 **Purity:** ≥95%

A solution in methanol **Stability:** ≥1 year at -20°C

Summary: A C-7 truncated analog of LXA_4 that is equiactive as LXA_4 in the inhibition of LTB_4-induced neutrophil chemotaxis (IC_{50} = 5 nM)

1 mg
5 mg
10 mg
100 mg



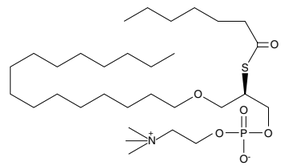
Heptanoyl thio-PC 10006809

MF: $C_{31}H_{64}NO_6PS$ **FW:** 609.9 **Purity:** ≥98%

A solution in ethanol **Stability:** ≥1 year at -20°C

Summary: A chromogenic PLA_2 substrate that contains an ether-linked saturated C16 moiety at the *sn*-1 position and a thiol ester at the *sn*-2 position

5 mg
10 mg
25 mg
50 mg



5(S)-HETE 34230

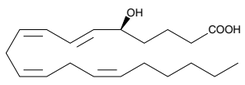
[70608-72-9]

MF: $C_{20}H_{32}O_3$ **FW:** 320.5 **Purity:** ≥98%

A solution in ethanol **Stability:** ≥1 year at -20°C

Summary: A product of 5-LO catalyzed oxidation of arachidonic acid

25 µg
50 µg
100 µg
250 µg



•Also Available: **5(S)-HETE-d_8** (334230)
5(S)-HETE Lipid Maps MS Standard (10007243)

15(R)-HETE 34710

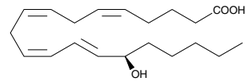
[83603-31-0]

MF: $C_{20}H_{32}O_3$ **FW:** 320.5 **Purity:** ≥98%

A solution in ethanol **Stability:** ≥2 years at -20°C

Summary: A product of arachidonic acid incubated with aspirin-inhibited COX-2

25 µg
50 µg
100 µg
250 µg



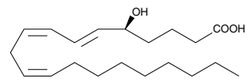
5(S)-HETrE 36230

MF: $C_{20}H_{34}O_3$ **FW:** 322.5 **Purity:** ≥98%

A solution in ethanol **Stability:** ≥1 year at -20°C

Summary: A product of 5-LO catalyzed oxidation of mead acid

25 µg
50 µg
100 µg
250 µg



15(S)-HETrE 36720

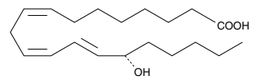
[92693-02-2]

MF: $C_{20}H_{34}O_3$ **FW:** 322.5 **Purity:** ≥98%

A solution in ethanol **Stability:** ≥2 years at -20°C

Summary: A hydroxy-trienoic acid resulting from 15-lipoxygenation of DGLA; inhibits human 5-LO with an IC_{50} value of 4.6 µM

25 µg
50 µg
100 µg
500 µg



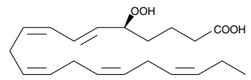
5(S)-HpEPE 42210

MF: $C_{20}H_{30}O_4$ **FW:** 334.5 **Purity:** ≥98%

A solution in ethanol **Stability:** ≥6 months at -80°C

Summary: A product of 5-LO catalyzed oxidation of EPA; can be further metabolized to LTA_5, a key intermediate in the formation of the 5-series LTs

25 µg
50 µg
100 µg
250 µg



5(S)-HpETE 44230

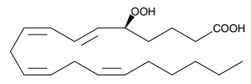
[71774-08-8]

MF: $C_{20}H_{32}O_4$ **FW:** 336.5 **Purity:** ≥98%

A solution in ethanol **Stability:** ≥6 months at -80°C

Summary: A product of 5-LO catalyzed oxidation of arachidonic acid; further metabolism by 5-LO gives LTA_4, a key intermediate in the formation of the 4-series LTs

25 µg
50 µg
100 µg
250 µg



•Also Available: **5(S)-HpETE Lipid Maps MS Standard** (10007257)

9(S)-HpODE 48410

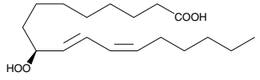
[29774-12-7]

MF: $C_{18}H_{32}O_4$ **FW:** 312.4 **Purity:** ≥98%

A solution in ethanol **Stability:** ≥6 months at -80°C

Summary: A monohydroxy PUFA produced by the action of arachidonate 5-LO on linoleic acid

50 µg
100 µg
500 µg
1 mg



HQL-79 10134

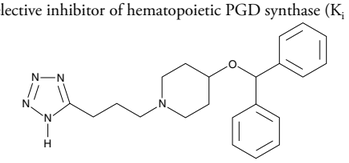
[162641-16-9]

MF: $C_{22}H_{27}N_5O$ **FW:** 377.5 **Purity:** ≥98%

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

Summary: A selective inhibitor of hematopoietic PGD synthase (K_i = 5 µM)

1 mg
5 mg
10 mg
100 mg



7-hydroxycoumarinyl Arachidonate 62910

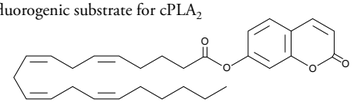
[161180-11-6] Umbelliferyl Arachidonate

MF: $C_{29}H_{36}O_4$ **FW:** 448.6 **Purity:** ≥98%

A solution in ethanol **Stability:** ≥1 year at -20°C

Summary: A fluorogenic substrate for $cPLA_2$

5 mg
10 mg
25 mg
50 mg

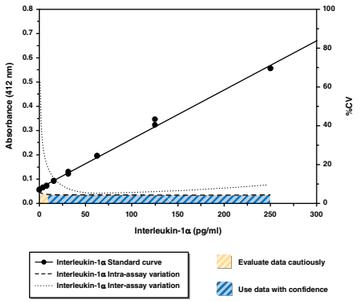


Interleukin-1α (human) EIA Kit 583301

Stability: ≥1 year at -20°C **Limit of Detection:** ~3.9 pg/ml

Summary: Cayman's IL-1α (human) EIA is an immunometric (*i.e.*, sandwich) EIA that permits IL-1α measurements within the range of 0-250 pg/ml

96 wells
480 wells

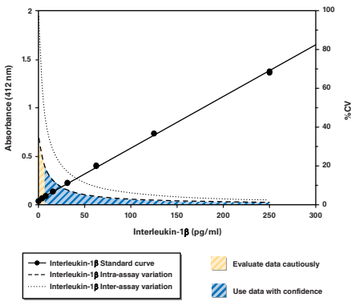


Interleukin-1β (human) EIA Kit 583311

Stability: ≥6 months at -20°C **Limit of Detection:** 3.9 pg/ml

Summary: Cayman's IL-1β (human) EIA is an immunometric (*i.e.*, sandwich) EIA that permits IL-1β measurements within the range of 0-250 pg/ml, typically with a limit of detection of 3.9 pg/ml.

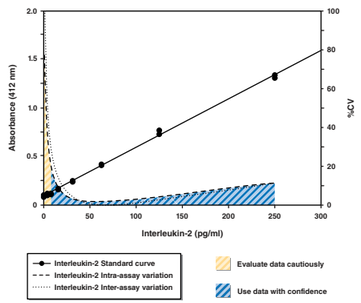
96 wells
480 wells



Interleukin-2 (human) EIA Kit 583321

Stability: ≥6 months at -20°C **Limit of Detection:** 15.6 pg/ml
Summary: Cayman's IL-2 assay is an immunometric 'sandwich' EIA that permits IL-2 measurements within the range of 0-250 pg/ml, typically with a limit of detection of 15.6 pg/ml. This assay provides a method for the sensitive, specific analysis of IL-2 in serum, plasma, or cell culture media.

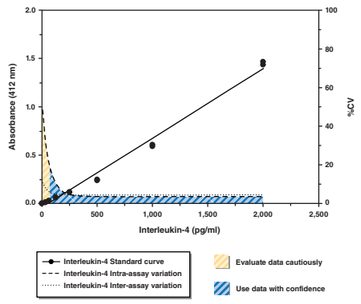
96 wells
480 wells



Interleukin-4 (human) EIA Kit 583341

Stability: ≥6 months at -20°C
Limit of Detection: 62.5 pg/ml (30 minutes) and 31.3 pg/ml (90 minutes)
Summary: Cayman's IL-4 assay is an immunometric 'sandwich' EIA that permits IL-4 measurements within the range of 0-2,000 pg/ml, typically with a limit of detection of 31 pg/ml. This assay provides a method for the sensitive, specific analysis of IL-4 in serum, plasma, or cell culture media.

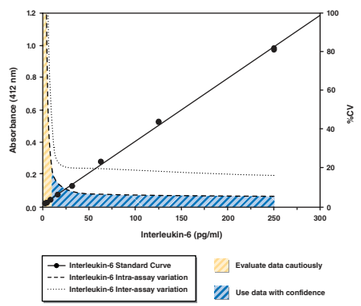
96 wells
480 wells



Interleukin-6 (human) EIA Kit 583361

Stability: ≥6 months at -20°C **Limit of Detection:** 7.8 pg/ml
Summary: Cayman's IL-6 (human) EIA is an immunometric (*i.e.,* sandwich) EIA that permits IL-6 measurements within the range of 0-250 pg/ml, typically with a limit of detection of 7.8 pg/ml.

96 wells
480 wells



Interleukin-33 (human) Monoclonal Antibody (Clone IL33305B) 10809

IL-1F11, IL-33, NF-HEV
A 1 mg/ml solution in PBS, pH 7.4 **Stability:** ≥ 6 months at -20°C
Summary: Antigen: recombinant human IL-33 • Host: mouse, clone IL33305B • Cross Reactivity: (+) human IL-33; (-) mouse IL-33 • Application(s): ELISA, IHC, IP, and WB • IL-33, a member of the IL-1 family of cytokines, is expressed by many cell types following pro-inflammatory stimulation, and is thought to be released on cell lysis.

50 µg
100 µg

Lane 1: Recombinant IL-33 (human) (His-tagged)
Lane 2: Recombinant IL-33 (human) (FLAG®-tagged)

Interleukin-33 Monoclonal Antibody (Clone IL33026B) 10811

IL-1F11, IL-33, NF-HEV
A 1 mg/ml solution in PBS, pH 7.4 **Stability:** ≥ 6 months at -20°C
Summary: Antigen: recombinant human IL-33 • Host: mouse, clone IL33026B • Cross Reactivity: (+) human and mouse IL-33 • Application(s): ELISA, IP, and WB • IL-33, a member of the IL-1 family of cytokines, is expressed by many cell types following pro-inflammatory stimulation, and is thought to be released on cell lysis.

50 µg
100 µg

Lane 1: Recombinant IL-33 (human) (His-tagged)
Lane 2: Recombinant IL-33 (mouse) (FLAG®-tagged)
Lane 3: Recombinant IL-33 (human) (FLAG®-tagged)

Interleukin-33 Monoclonal Antibody (Clone IL333068A) 10810

IL-1F11, IL-33, NF-HEV
A 1 mg/ml solution in PBS, pH 7.4 **Stability:** ≥ 6 months at -20°C
Summary: Antigen: recombinant human IL-33 • Host: mouse, clone IL333068A • Cross Reactivity: (+) human IL-33 • Application(s): ELISA and WB • IL-33, a member of the IL-1 family of cytokines, is expressed by many cell types following pro-inflammatory stimulation, and is thought to be released on cell lysis.

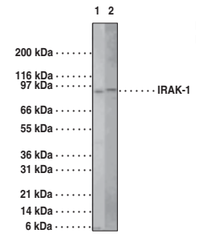
50 µg
100 µg

Lane 1: Recombinant IL-33 (human) (His-tagged)
Lane 2: Recombinant IL-33 (human) (FLAG®-tagged)
Lane 3: Recombinant IL-33 (mouse) (FLAG®-tagged)

IRAK-1 Polyclonal Antibody 13843

Protein G-purified IgG **Stability:** ≥ 6 months at 4°C
Summary: Antigen: synthetic peptide corresponding to human IRAK-1 amino acids 700-712 • Host: rabbit • Cross Reactivity: (+) human and mouse IRAK-1; (-) IRAK-2 • Application(s): IP and WB • IRAK-1 is associated with the IL-1 receptor subunits IL-1RI and IL-1RAcP after IL-1 binding and serves as a signaling molecule to mediate the IL-1 response. IRAK-1 mediates a signaling cascade leading to NF-κB activation by members of the IL-1 family including IL-1 and IL-18.

1 ea

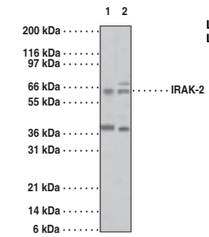


Lane 1: HeLa cell lysate
Lane 2: NIH 3T3 cell lysate

IRAK-2 Polyclonal Antibody 13844

Protein G-purified IgG **Stability:** ≥ 6 months at 4°C
Summary: Antigen: synthetic peptide from human IRAK-2 • Host: rabbit • Cross Reactivity: (+) human and mouse IRAK-2 • Application(s): WB • IRAK-2 is a serine/threonine protein kinase that mediates NF-κB activation by members of the IL-1 family including IL-1 and IL-18.

1 ea

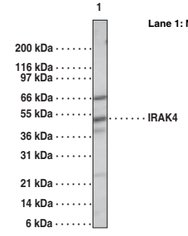


Lane 1: Human K562 cell lysate
Lane 2: Mouse RAW cell lysate

IRAK-4 Polyclonal Antibody 13845

Protein G-purified IgG **Stability:** ≥ 6 months at 4°C
Summary: Antigen: synthetic peptide corresponding to a mixture of murine IRAK-4 amino acids 38-54 and 120-136 • Host: rabbit • Cross Reactivity: (+) human and mouse IRAK-4 • Application(s): IP and WB • IRAK-4 is an adaptor protein that is important for activation of NF-κB and MAPK pathways following LPS binding to TLRs. Mice lacking IRAK4 are resistant to lethal doses of LPS and are also severely impaired in their responses to viral and bacterial challenges.

1 ea

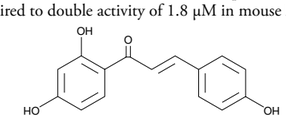


Lane 1: NIH 3T3 cell lysate

Isoliquiritigenin 10739

[961-29-5] GU 17, ISL
MF: $C_{15}H_{12}O_4$ **FW:** 256.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A flavonoid found in licorice root that displays antioxidant, anti-inflammatory, and antitumor activities; induces quinone reductase-1 with a concentration required to double activity of 1.8 µM in mouse hepatoma cells

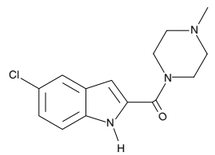
1 mg
5 mg
10 mg
50 mg



JNJ-7777120 10011925

[459168-41-3]
MF: $C_{14}H_{16}ClN_3O$ **FW:** 277.8 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent and selective histamine H4 receptor antagonist, with a K_i value of approximately 4 nM against the human, mouse, and rat H4 receptors; inhibits mast cell chemotaxis induced by 10 µM histamine (IC_{50} = 40 nM), reduces neutrophil influx in mouse peritonitis models (10 mg/kg s.c.), and impairs eosinophil and lymphocyte influx into airways during allergic airway inflammation

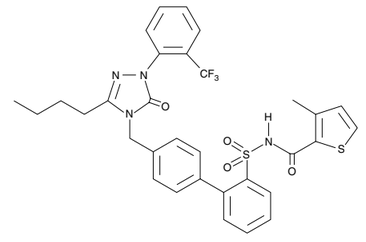
1 mg
5 mg
10 mg
50 mg



L-161,982 10011565

[147776-06-5]
MF: $C_{32}H_{29}F_3N_4O_4S_2$ **FW:** 654.2 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent and selective EP_4 receptor antagonist (K_i = 24 nM); reverses the anti-inflammatory action of PGE_2 in LPS-activated human macrophages at 100 nM

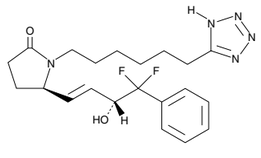
1 mg
5 mg
10 mg
50 mg



L-902,688 10007712

[634193-54-7]
MF: $C_{21}H_{27}F_2N_5O_2$ **FW:** 419.5 **Purity:** ≥98%
A solution in ethanol **Stability:** ≥1 year at -20°C
Summary: A potent and selective agonist of the human EP_4 receptor with a K_i value of 0.38 nM and an EC_{50} value of 0.6 nM; induces thermal hyperalgesia when injected into guinea pig forepaw and increases vasodilation of human pulmonary vein

500 µg
1 mg
5 mg
10 mg



vol. 13 In

Thomas G. Brock, Ph.D.

The Strange Side of Leukotriene Synthesis

The maturation of a scientist requires insight, imagination, and flexibility. One's earliest introduction to science may involve learning names of plants, animals, or chemicals. With time, the complexity of science adds challenge, intrigue, and, most importantly, puzzling questions. Why are some plants hermaphroditic and how can they change their sexuality over time? Why is aspirin good for your headache, bad for your stomach, and potentially lethal for some asthmatics? The experienced scientist understands that nature is strange and learns to expect the unexpected.

So it is with biochemists and cell biologists. They first learn that an enzyme converts substrate to product, or that DNA is transcribed to RNA in the nucleus, which in turn is translated to protein in the cytoplasm. Only later do they learn the complexity of these systems and, with time, how little we actually understand about, say, how calcium levels are regulated within the nucleus and how calcium fluxes affect nuclear enzymes or gene transcription. Or, what controls fatty acid movement within cells and how do they modulate transcriptional and epigenetic processes? Calcium fluxes and fatty acid transport intersect in the wild world of leukotriene synthesis. Here are some of the details.

The 5-LO Pathway

The biosynthesis of leukotrienes (LT) can be outlined rather simply. The polyunsaturated fatty acid arachidonic acid (AA) is first oxygenated on the fifth carbon by 5-lipoxygenase (5-LO) in conjunction with its activating protein, FLAP, to give 5-hydroperoxy eicosapentaenoic acid (5-HpETE), as shown in Figure 1.[1] 5-LO, with FLAP, then catalyzes a second step, the dehydration of 5-HpETE to the intermediate LTA_4. LTA_4 can be combined with water to generate the 5,12-dihydroxy molecule, LTB_4, or conjugated with glutathione on carbon six to produce LTC_4. These reactions are mediated by LTA_4 hydrolase (LTA_4H) and LTC_4 synthase (LTC_4S), respectively. Both LTB_4 and LTC_4 are then secreted from cells, where the glutathione moiety on LTC_4 can be sequentially cleaved to produce LTD_4 and LTE_4. Specific receptors localized on distinct cell types evoke LT-specific responses: LTB_4 promotes adherence, chemotaxis, and activation of leukocytes and initiates the synthesis of pro-inflammatory mediators, while LTC_4, LTD_4, and LTE_4 direct the contraction of smooth muscle, leading to vaso- and bronchoconstriction as well as edema.

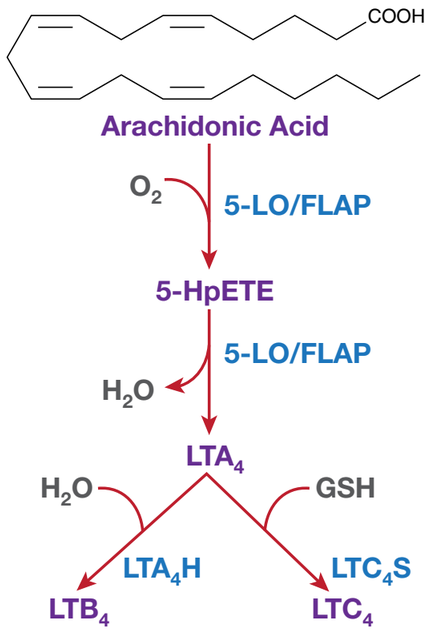


Figure 1. The pathway for the biosynthesis of LTs from arachidonic acid

The substrate for LT biosynthesis, AA, is stored in membrane phospholipids and is released by phospholipases (PL), most notably cytoplasmic PLA_2 ($cPLA_2$). Both $cPLA_2$ and 5-LO are soluble in resting cells, activated by a rise in intracellular calcium, and rapidly associate with nuclear and perinuclear membranes in the presence of calcium. Thus, appropriate cell stimulation initiates an acute release of AA from membranes, leading to the production of LTs in a matter of minutes.

Weird Lipid Behavior

Polyunsaturated fatty acids, like AA, 5-HpETE, LTA_4, and LTB_4, are lipids, and, as such, might be expected to pass through or partition into membranes. Indeed, long chain fatty acids pass through membranes by a 'flip-flop' mechanism.[2] Intuitively, one might anticipate that AA, supplied externally to cells, might accumulate at the plasma membrane. However, it has long been known that exogenously added AA moves rapidly to the nuclear and perinuclear membranes. Naturally, fatty acid-binding proteins (FABP) bind fatty acids, including AA, 5-HpETE, and LTA_4. Intriguingly, FABPs can shuttle their cargo to, or even into, the nucleus.[3] While FABPs have been shown to stabilize LTA_4,[4] little is known about the importance of FABP transport in LT synthesis.

The end products, LTB_4 and LTC_4, are actively exported from cells by energy-dependent transporters. LTC_4 is exported by the ATP-binding cassette (ABC) transporter ABCC1, also known as multidrug resistance-associated protein 1 (MRP-1). Similarly, another important AA derivative, prostaglandin E_2, is exported by the ABC transporter ABCC4, suggesting that a related protein might mediate the release of LTB_4 from cells. Perhaps more unusually, AA is rapidly transported both out of and into cells by energy-dependent tranporters.[5,6] In fact, PLA_2 activity (inside cells) can be monitored by measuring the amount of labeled AA that is 'trapped' by albumin outside of the cell following cell stimulation. The inclusion of such a trap greatly impairs the production of LTs, suggesting that AA is exported from cells rapidly following its release from membranes. Moreover, the intermediate LTA_4 is rapidly released from neutrophils, only to be taken up by neighboring neutrophils and metabolized to LTB_4.[7] It is not known if 5-HpETE can be similarly moved out of and into cells. However, the movement of AA and LTA_4 forces us to consider LT synthesis beyond the cytoplasm of single cells.

Leukotrienes were so named because they were first isolated from leukocytes, which express 5-LO. Such cells move in relatively low numbers through the circulation but accumulate at sites of inflammation. Moreover, in inflamed tissues, leukocytes must abut other cell types that lack 5-LO but express LTA_4H or LTC_4S, such as epithelial cells and smooth muscle cells, respectively. Thus, LTA_4 donated by leukocytes will be processed to the final LT product by nearest neighbors. Non-leukocytes typically contain $cPLA_2$, so they can provide AA to leukocytes. There is abundant evidence that different cell types share either AA or LTA_4 to produce LTs through such a transcellular mechanism.[8,9] Thus, LT synthesis can be viewed as a multicellular process, with the amount and type of product (LTB_4 *vs.* LTC_4) reflecting the overall cellular profile.

Complex Enzymes

While lipids move to the plasma membrane and beyond, the actions of the enzymes involved in LT synthesis center on the two membranes of the nuclear envelope, as well as the endoplasmic reticulum (which is an extension of the outer nuclear membrane). As noted earlier, $cPLA_2$ and 5-LO are soluble in resting cells and associate with nuclear membranes when activated by a rise in calcium (Figure 2). AA released by $cPLA_2$ may be exported or delivered to 5-LO by FLAP. FLAP exists as a monomer or homodimer on both inner and outer membranes of the nuclear envelope, and also as a heterodimer with LTC_4S on the outer membrane only.[10,11] FLAP is a fatty acid transport protein which facilitates delivery of AA to 5-LO.[12] It is not known whether FLAP also funnels LTA_4, produced by 5-LO, to LTC_4S, but clearly the FLAP-LTC_4S dimer efficiently produces LTC_4, while soluble LTA_4H generates LTB_4. Protein kinase A (PKA) inhibits LT synthesis by phosphorylating Ser^{523} on 5-LO.[13]

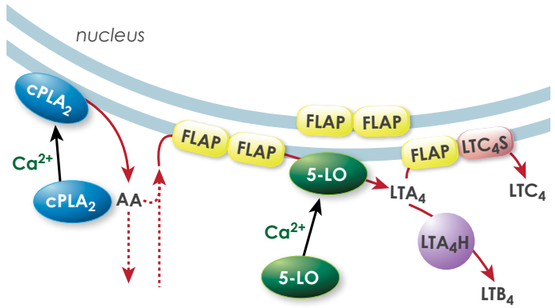


Figure 2. Biosynthesis of LTs from AA in the cytoplasm

To complicate matters, 5-LO can be imported into and exported from the nucleus.[14,15] Import is regulated by three independent nuclear import sequences, which allow graded levels of import.[16] Phosphorylation on Ser^{523} by PKA inhibits import, while phosphorylation on Ser^{271} inhibits export.[17,18] Perhaps most importantly, positioning 5-LO within the nucleus increases the synthesis of LTB_4 but strongly decreases LTC_4 generation.[14,19,20] As described above, AA, either released from $cPLA_2$ at the outer membrane or derived from outside the cell, is (presumably) imported through nuclear pores by FABP, delivered to 5-LO at the inner membrane by FLAP, and metabolized to LTA_4. Note that the rise in nuclear calcium, to activate 5-LO must be coordinated with that in the cytoplasm which activated $cPLA_2$. LTA_4 produced by 5-LO can then be converted to LTB_4 by nuclear LTA_4H or, less efficiently, processed by LTC_4S on the outer membrane of the nuclear envelope. While LTA_4H has been detected within the nucleus of many cell types, it has only been observed in the cytoplasm of neutrophils.[21,22] Perhaps the production of LTA_4 by nuclear 5-LO, in the absence of nuclear LTA_4H, helps explain why neutrophils export large amounts of LTA_4.

Nuclear LT Signaling?

Why are AA and LTA_4 exported from cells, only to be taken up by neighbors and imported again, into the nucleus of all places? Why are 5-LO and LTA_4H positioned within the nucleoplasm in some cases and in the cytoplasm in others? Polyunsaturated fatty acids and their oxygenated derivatives are known to act as co-factors for enzymes and activators of nuclear receptors (*e.g.*, peroxisomal proliferator-activated receptor-γ). The fundamental basis

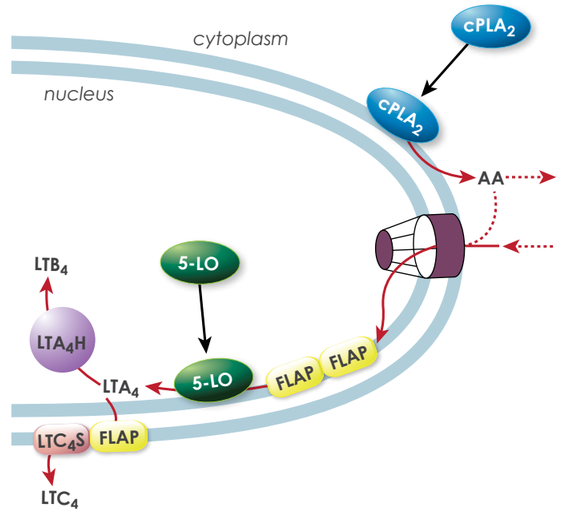


Figure 3. Biosynthesis of LTs from AA within the nucleus

for the specificity of these interactions, like the binding of LTs with their G protein-coupled receptors, centers on the three dimensional structure of each lipid. Recently, there has been an explosion of interest in the protein complexes which act within the nucleus, particularly at the level of the nucleosome, and how they control gene expression. Perhaps neutrophils donate LTA_4 to epithelial cells, or other cells which have nuclear LTA_4H but lack 5-LO, to generate an important protein complex modulator, LTB_4. Similarly, 5-LO products, generated within the nucleus, may act as co-factors of protein complexes involved in the function of longer-lived leukocytes, like monocytes, macrophages, and mast cells. The more imaginative scientist will likely see additional possibilities.

References

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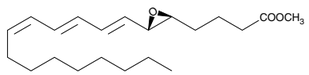
Leukotriene A_3 methyl ester 20009

[83851-38-1]
MF: $C_{21}H_{34}O_3$ **FW:** 334.5 **Purity:** ≥97%
A solution in hexane containing 1% triethylamine **Stability:** ≥1 year at -80°C
Summary: A putative intermediate in the biosynthesis of 3-series LTs derived from 5,8,11-eicosatrienoic acid *via* the 5-LO pathway

25 µg
50 µg
100 µg
500 µg



Leukotriene A_4 Hydrolase (human recombinant) 10007817

LTA_4H
M_r: ~69 kDa **Purity:** ≥90%
Supplied in: 100 mM Tris, pH 8.0, containing 100 mM potassium chloride and 20% glycerol
Summary: Recombinant C-terminal His-tagged enzyme expressed in *E. coli* • A bifunctional zinc metalloenzyme that converts LTA_4 into LTB_4, a potent neutrophil chemoattractant; potential drug target for a variety of indications associated with leukocyte infiltration to sites of inflammation; has application for the screening of inhibitors of LTB_4 synthesis

25 µg
50 µg
100 µg

Leukotriene A_4 Hydrolase Polyclonal Antibody 160250

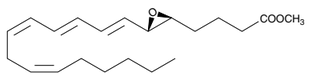
Protien-A purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human recombinant LTA_4 hydrolase • Host: rabbit • Cross Reactivity: (+) human LTA_4 hydrolase • Application(s): WB • LTA_4 hydrolase has been cloned from a variety of species including human, rat, and guinea pig. These species exhibit ~90% homology at the amino acid level. Human LTA_4 hydrolase has a calculated molecular mass of 69 kDa based on the deduced amino acid sequence.

500 µl

Leukotriene A_4 methyl ester 20010

[73466-12-3]
MF: $C_{21}H_{32}O_3$ **FW:** 332.5 **Purity:** ≥97%
A solution in hexane containing 1% triethylamine **Stability:** ≥1 year at -80°C
Summary: A stable formulation of LTA_4, the intermediate in LTs derived from arachidonic acid by 5-LO

25 µg
50 µg
100 µg
500 µg

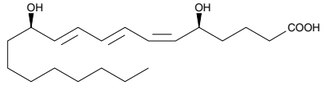


•Also Available: **Leukotriene A_4-d_5 methyl ester** (10006197)

Leukotriene B_3 20109

[88099-35-8]
MF: $C_{20}H_{34}O_4$ **FW:** 338.5 **Purity:** ≥97%
A solution in ethanol **Stability:** ≥1 year at -20°C
Summary: The LTA hydrolase metabolite of LTA_3 in the LT biosynthetic pathway

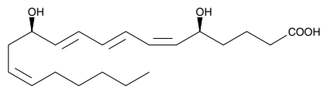
25 µg
50 µg
100 µg
500 µg



Leukotriene B_4 20110

[71160-24-2]
MF: $C_{20}H_{32}O_4$ **FW:** 336.5 **Purity:** ≥97%
A solution in ethanol **Stability:** ≥1 year at -20°C
Summary: A key dihydroxy fatty acid derived from arachidonic acid through the 5-LO pathway; promotes a number of leukocyte functions including chemotaxis and chemokinesis at subnanomolar concentrations

25 µg
50 µg
100 µg
1 mg

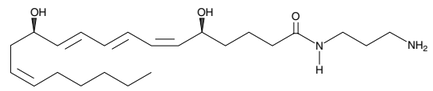


•Also Available: **Leukotriene B_4-d_4** (320110)
Leukotriene B_4 Lipid Maps MS Standard (10007240)
12-oxo Leukotriene B_4 (20140)

Leukotriene B_4-3-aminopropylamide 20114

[89596-43-0]
MF: $C_{23}H_{40}N_2O_3$ **FW:** 392.6 **Purity:** ≥95%
A solution in ethanol **Stability:** ≥1 year at -20°C
Summary: An analog of LTB_4 that binds to the BLT_1 and BLT_2 receptors with K_i values of 5.1 and 1,227 nM, respectively

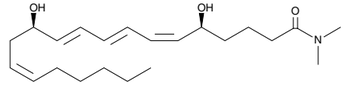
25 µg
50 µg
100 µg
500 µg



Leukotriene B_4 dimethyl amide 20115

[83024-92-4]
MF: $C_{22}H_{37}NO_3$ **FW:** 363.5 **Purity:** ≥97%
A solution in methanol **Stability:** ≥2 years at -20°C
Summary: A moderate inhibitor of LTB_4-induced degranulation of human neutrophils (K_i = 130 nM)

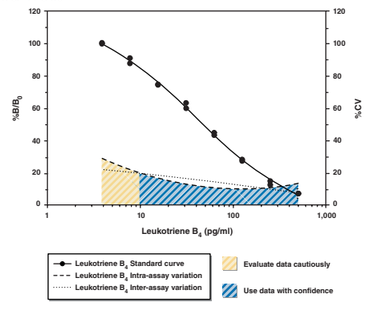
25 µg
50 µg
100 µg
250 µg



Leukotriene B_4 EIA Kit 520111

Stability: ≥6 months at -20°C
Sensitivity: 50% B/B_0: 50 pg/ml • 80% B/B_0: 13 pg/ml
Summary: LTB_4 is synthesized from arachidonic acid by the combined action of 5-LO and LTA_4 hydrolase. LTB_4 has long been recognized as a potent mediator of inflammation. It stimulates a number of leukocyte functions, including aggregation, stimulation of ion fluxes, enhancement of lysosomal enzyme release, superoxide anion production, chemotaxis, and chemokinesis. In subnanomolar ranges (3.9×10^{-10} M), LTB_4 causes chemotaxis and chemokinesis in human PMNLs.

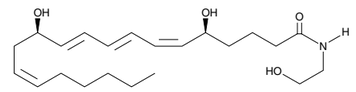
96 strip/solid wells
480 strip/solid wells



Leukotriene B_4 Ethanolamide 20112

MF: $C_{22}H_{37}NO_4$ **FW:** 379.5 **Purity:** ≥97%
A solution in ethanol **Stability:** ≥1 year at -20°C
Summary: A theoretical 5-LO metabolite of AEA; acts as a potent antagonist of the human BLT_1 receptor (K_i = 1.22 nM)

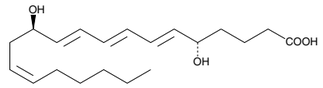
25 µg
50 µg
100 µg
500 µg



6-*trans* Leukotriene B_4 35250

[71652-82-9] All trans LTB_4, 5(S),12(R)-DiHETE
MF: $C_{20}H_{32}O_4$ **FW:** 336.5 **Purity:** ≥97%
A solution in ethanol **Stability:** ≥1 year at -20°C
Summary: A non-enzymatic hydrolysis product of LTA_4 with reduced activity compared to LTB_4; also produced by oxidative decomposition of CysLTs such as LTC_4 in the presence of myeloperoxidase and hypochlorous acid

25 µg
50 µg
100 µg
250 µg

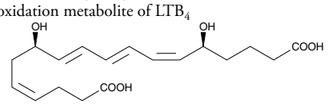


•Also Available: **6-*trans* Leukotriene B_4 Lipid Maps MS Standard** (35250)
6-*trans*-12-*epi* Leukotriene B_4 (35265)

18-carboxy dinor Leukotriene B_4 20170

[102674-12-4]
MF: $C_{18}H_{26}O_6$ **FW:** 338.4 **Purity:** ≥97%
A solution in ethanol **Stability:** ≥1 year at -20°C
Summary: A β-oxidation metabolite of LTB_4

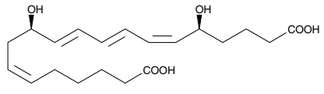
25 µg
50 µg
100 µg
250 µg



20-carboxy Leukotriene B_4 20180

[80434-82-8]
MF: $C_{20}H_{30}O_6$ **FW:** 366.5 **Purity:** ≥97%
A solution in ethanol **Stability:** ≥2 years at -20°C
Summary: A metabolite of LTB_4 in human neutrophils with significantly reduced biological activity

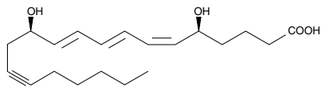
25 µg
50 µg
100 µg
250 µg



14,15-dehydro Leukotriene B_4 20150

[114616-11-4]
MF: $C_{20}H_{30}O_4$ **FW:** 334.5 **Purity:** ≥97%
A solution in ethanol **Stability:** ≥1 year at -80°C
Summary: An LTB_4 receptor antagonist that has a higher binding affinity for BLT_1 (K_i = 27 nM) compared to BLT_2 (K_i = 473 nM); inhibits LTB_4-induced release of lysozymes from rat PMNLS with an IC_{50} value of 1 µM

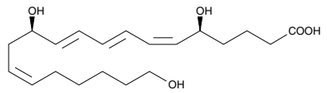
25 µg
50 µg
100 µg
500 µg



20-hydroxy Leukotriene B_4 20190

[79516-82-8]
MF: $C_{20}H_{32}O_5$ **FW:** 352.5 **Purity:** ≥97%
A solution in ethanol **Stability:** ≥1 year at -20°C
Summary: A metabolite of LTB_4 in human neutrophils; inhibits LTB_4-induced degranulation of human neutrophils (K_i = 13.3 nM)

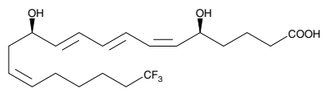
25 µg
50 µg
100 µg
500 µg



20-trifluoro Leukotriene B_4 20195

[115178-97-7]
MF: $C_{20}H_{29}F_3O_4$ **FW:** 390.4 **Purity:** ≥97%
A solution in ethanol **Stability:** ≥1 year at -20°C
Summary: A synthetic analog of LTB_4 resistant to metabolism by ω-oxidation; equipotent to LTB_4 in chemotactic activity (EC_{50} = 3 nM); inhibits LTB_4 - induced degranulation of neutrophils (IC_{50} = 1-2 nM)

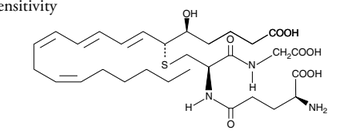
25 µg
50 µg
100 µg
500 µg



Leukotriene C_4 20210

[72025-60-6]
MF: $C_{30}H_{47}N_3O_9S$ **FW:** 625.8 **Purity:** ≥97%
A solution in ethanol:water (95:5) **Stability:** ≥1 year at -80°C
Summary: The parent CysLT produced by the LTC_4 synthase-catalyzed conjugation of glutathione to LTA_4; potent inducer of bronchoconstriction and enhanced vascular permeability that contributes to the pathogenesis of asthma and acute allergic hypersensitivity

25 µg
50 µg
100 µg
500 µg

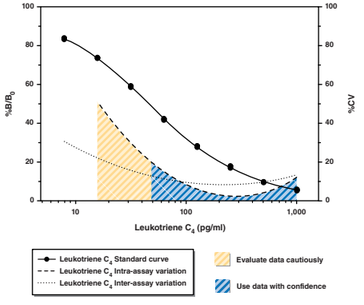


•Also Available: **Leukotriene C_4-d_5** (10006198)
Leukotriene C_4 Lipid Maps MS Standard (10007241)

Leukotriene C_4 EIA Kit 520211

Stability: ≥6 months at -80°C
Sensitivity: 50% B/B_0: 45 pg/ml • 80% B/B_0: 10 pg/ml
Summary: Cayman's LTC_4 Assay is a competitive EIA that can best be used for the quantification of LTC_4 in select sample types. Cultured cells synthesizing LTC_4 will generally release it into the medium where it will accumulate without further metabolism. Plasma levels of LTC_4 are virtually undetectable.

96 strip/solid wells
480 strip/solid wells



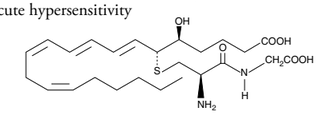
•Also Available: **14,15-Leukotriene C_4 EIA Kit** (10006748)

Leukotriene D_4 20310

[73836-78-9]

MF: $C_{25}H_{40}N_2O_6S$ **FW:** 496.7 **Purity:** ≥97%
A solution in ethanol **Stability:** ≥1 year at -80°C
Summary: The first CysLT metabolite of LTC_4; acts as a potent inducer of bronchoconstriction and vascular permeability that contributes to the pathogenesis of asthma and acute hypersensitivity

25 µg
50 µg
100 µg
1 mg



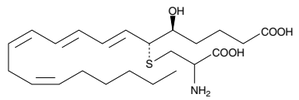
•Also Available: **Leukotriene D_4-d_5** (10006199)

Leukotriene E_4 20410

[75715-89-8]

MF: $C_{23}H_{37}NO_5S$ **FW:** 439.6 **Purity:** ≥97%
A solution in ethanol **Stability:** ≥1 year at -80°C
Summary: Metabolite of LTD_4 and one of the constituents of slow-reacting substance of anaphylaxis; considerably less active (8- to 12-fold) than LTC_4 in the biological activities characteristic of CysLTs; urinary excretion of LTE_4 is often used as an indicator of asthma

25 µg
50 µg
100 µg
1 mg

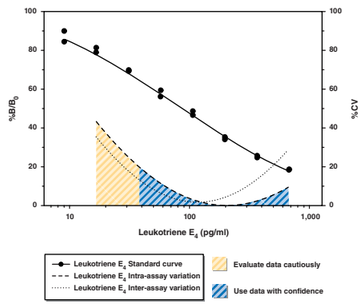


•Also Available: **Leukotriene E_4-d_5** (10007858)
Leukotriene E_4 Lipid Maps MS Standard (10007242)

Leukotriene E_4 EIA Kit 520411

Stability: ≥6 months at -80°C
Sensitivity: 50% B/B_0: 100 pg/ml • 80% B/B_0: 25 pg/ml
Summary: Cayman's LTE_4 EIA is a competitive assay that can be used for quantification of LTE_4 in urine, plasma, serum, whole blood, as well as other heterogeneous mixtures such as lavage fluids and aspirates and other sample matrices.

96 strip/solid wells
480 strip/solid wells

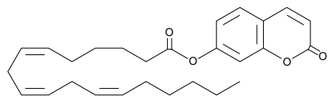


Licofelone 10007692

[156897-06-2] ML 3000

MF: $C_{23}H_{22}ClNO_2$ **FW:** 379.9 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A dual inhibitor of COX and LO pathways, that decreases levels of PGE_2, LTB_4, and lipoxins and prevents LPS-stimulated IL-1β expression; IC_{50}s values are 0.16 and 0.23 µM, respectively, for inhibition of human thrombocyte COX and human 5-LO; causes little or no damage to the gastric mucosa in rabbit parietal cells, unlike other NSAIDs

5 mg
10 mg
25 mg
50 mg

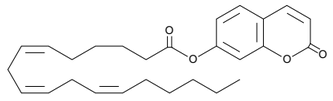


7-hydroxycoumarinyl-γ-Linolenate 10556

[161180-12-7] Umbelliferyl-γ-Linolenate

MF: $C_{27}H_{34}O_4$ **FW:** 422.6 **Purity:** ≥98%
A solution in ethanol **Stability:** ≥1 year at -20°C
Summary: A γ-linolenic acid ester of 7-hydroxycoumarin that behaves as a substrate for $cPLA_2$

5 mg
10 mg
25 mg
50 mg

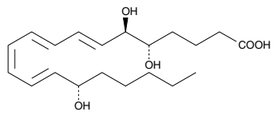


5(S),6(R)-Lipoxin A_4 90410

[89663-86-5] 5(S),6(R),15(S)-TriHETE

MF: $C_{20}H_{32}O_5$ **FW:** 352.5 **Purity:** ≥95%
A solution in ethanol **Stability:** ≥1 year at -80°C
Summary: A trihydroxy fatty acid containing a conjugated tetraene produced by the metabolism of 15-HETE or 15-HpETE with human leukocytes; promotes leukocyte activation, chemotaxis effects, natural killer cell inhibition, and monocyte migration and adhesion

25 µg
50 µg
100 µg
250 µg



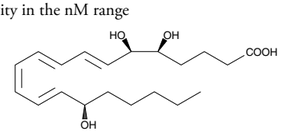
•Also Available: **5(S),6(R)-Lipoxin A_4-d_4** (10007737)
5(S),6(R)-Lipoxin A_4 Lipid Maps MS Standard (10007271)
5(S),6(R)-Lipoxin A_4 methyl ester (10033)
5(S),6(S)-Lipoxin A_4 (10049)

5(S),6(R),15(R)-Lipoxin A_4 90415

[171030-11-8] AT-LXA_4, 15-epi Lipoxin A_4

MF: $C_{20}H_{32}O_5$ **FW:** 352.5 **Purity:** ≥95%
A solution in ethanol **Stability:** ≥1 year at -80°C
Summary: An aspirin-triggered LX that inhibits LTB_4-induced chemotaxis, adherence, and transmigration of neutrophils with twice the potency of LXA_4, demonstrating activity in the nM range

25 µg
50 µg
100 µg
250 µg

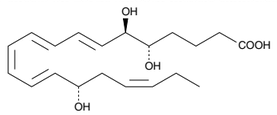


Lipoxin A_5 10011453

[110657-98-2]

MF: $C_{20}H_{30}O_5$ **FW:** 350.5 **Purity:** ≥95%
A solution in ethanol **Stability:** ≥1 year at -80°C
Summary: A 5-series lipoxin derived from EPA; contracts pulmonary parenchymal strips from guinea pig with similar potency to that of LXA_4 and LXB_4, yet does not exert the vasodilatory effects on aortic smooth muscle exhibited by LXA_4 and LXB_4

25 µg
50 µg
100 µg
500 µg

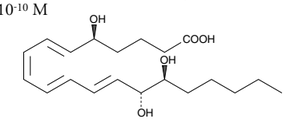


5(S),14(R)-Lipoxin B_4 90420

[98049-69-5]

MF: $C_{20}H_{32}O_5$ **FW:** 352.5 **Purity:** ≥95%
A solution in ethanol **Stability:** ≥1 year at -80°C
Summary: A positional isomer of LXA_4 produced by the metabolism of 15-HETE or 15-HpETE by human leukocytes; inhibits PMN migration stimulated by LTB_4 at a concentration of 10^{-7} M and inhibits LTB_4-induced adhesion of PMNs with an IC_{50} value of ~3 x 10^{-10} M

25 µg
50 µg
100 µg
500 µg



5-Lipoxygenase (human recombinant) 60402

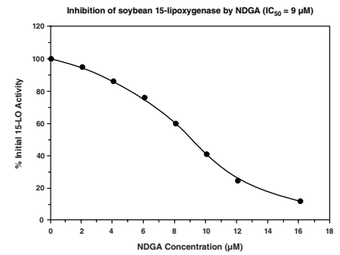
MF: Monomer M_r: 78 kDa **Purity:** 16,000 x g supernatant
Supplied in: A solution in 100 mM Tris-HCl, pH 8.0, containing 5 mM EGTA, 1mM $CaCl_2$, and 30% glycerol
Summary: Recombinant enzyme expressed in Sf21 cells • Catalyzes the formation of 5(S)-HpETE from arachidonic acid as well as its subsequent conversion to leukotriene A_4; localized in the cytosol of resting human and rat peripheral blood neutrophils or in the nuclesus in rat basophilic leukemia cells and human alveolar macrophages; translocates to the nuclear membrane to associate with FLAP upon cell stimulation

500 units
1 Kunit
2.5 Kunit
5 Kunit

Lipoxygenase Inhibitor Screening Assay Kit 760700

Stability: ≥1 year at 4°C
Summary: This assay kit provides an accurate and convenient method for screening LO inhibitors. This assay measures the hydroperoxides generated from the incubation of a LO (5-, 12-, or 15-LO) with either arachidonic or linoleic acid.

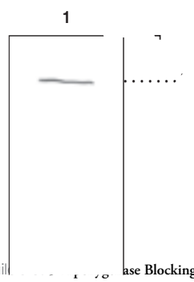
96 wells



5-Lipoxygenase Polyclonal Antibody 160402

Peptide affinity-purified IgG **Stability:** ≥2 years at -20°C
Summary: Antigen: human and rat 5-LO amino acids 130-149 • Host: rabbit • Cross Reactivity: (+) human, rat, mouse, hamster, and porcine 5-LO; (-) 12-LO and 15-LO • Application(s): ICC, IHC, and WB • 5-LO catalyzes the formation of 5(S)-HpETE from arachidonic acid as well as its subsequent conversion to LTA_4

500 µl



•Also Avail… …ase Blocking Peptide (360402)

5-Lipoxygenase (Phospho-Ser[523]) Polyclonal Antibody 10007820

Peptide affinity-purified **Stability:** ≥1 year at -20°C
Summary: Antigen: phosphopeptide corresponding to amino acid residues surrounding phospho-Ser^{523} of human 5-LO • Host: rabbit • Cross Reactivity: (+) human, rat, and non-human primate 5-LO • Application(s): WB • 5-LO enzyme plays a key role in regulating the production of LTs. Its activity is regulated by PKA phosphorylation at serine-523. Under normal conditions, this phosphorylation may be important in limiting inflammation. Abnormal signaling through cAMP and PKA may contribute to a variety of diseases, including those characterized by chronic inflammation.

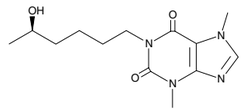
100 µl

(R)-Lisofylline 13616

[100324-81-0] (-)-Lisofylline, (R)-LSF

MF: $C_{13}H_{20}N_4O_3$ **FW:** 280.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent inhibitor of the generation of phosphatidic acid (IC_{50} = 0.6 µM) from cytokine-activated lysophosphatidic acyl transferase, which has been shown to protect mice from endotoxic shock; suppresses the production of the proinflammatory cytokine IFN-γ, inhibits IL-12 signaling, and enhances glucose-stimulated β-cell insulin secretion; reduces onset of diabetes in a non-obese diabetic mouse model

1 mg
5 mg
10 mg
25 mg

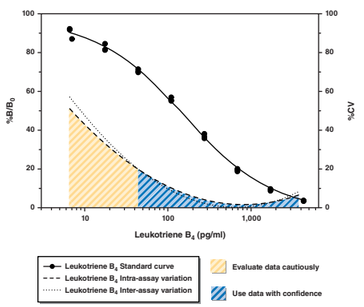


•Also Available: **(±)-Lisofylline** (10010785)
(S)-Lisofylline (13617)

Luminex® Leukotriene B_4 Kit 500260

Stability: ≥1 year at -20°C
Sensitivity: 50% B/B_0: 138 pg/ml • 80% B/B_0: 24 pg/ml
Summary: LTB_4 is a potent mediator of inflammation that stimulates a number of leukocyte functions, including aggregation, stimulation of ion fluxes, enhancement of lysosomal enzyme release, superoxide anion production, chemotaxis, and chemokinesis.

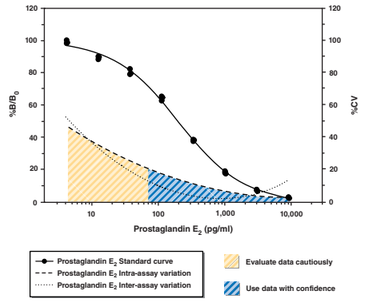
1 ea



Luminex® Prostaglandin E_2 Kit 10007501

Stability: ≥1 year at -20°C
Sensitivity: 50% B/B_0: 180 pg/ml • 80% B/B_0: 35 pg/ml
Summary: Cayman's Luminex® PGE_2 is the first of its kind for the measurement of PGE_2 using Luminex® xMAP® technology. For this application microspheres have been coated with Cayman's high-affinity PGE_2 monoclonal antibody. The assay is based on the competition between PGE_2 and a PGE_2-phycoerytherin conjugate (PGE_2 tracer) for the monoclonal antibody binding sites on the microsphere beads.

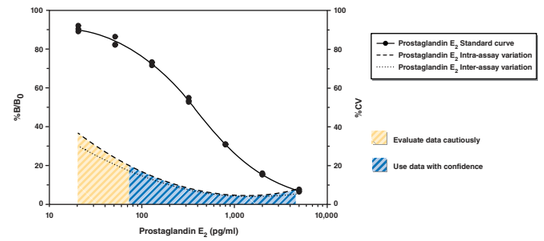
1 ea

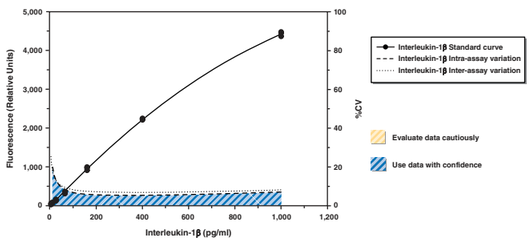


Luminex® Prostaglandin E_2/ Interleukin-1β Duplex Kit 10009597

Stability: ≥1 year at -20°C
PGE_2 Sensitivity: 50% B/B_0: 358 pg/ml • 80% B/B_0: 72 pg/ml
Summary: PGE_2 and IL-1β are inflammatory mediators that often co-exist both *in vivo* and *in vitro*. Cayman's PGE_2-IL-1β Luminex® assay allows users to measure PGE_2 and IL-1β simultaneously for the first time. The unique feature of this assay is the combination of a 'sandwich'-type assay for IL-1β and a competitive assay for PGE_2. The assay requires no wash steps and can be completed in about 6 hours.

1 ea

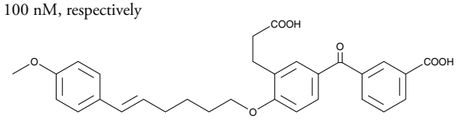




LY223982 10010024

[117423-74-2] CGS 23131, SKF 107234
MF: $C_{30}H_{30}O_7$ **FW:** 502.6 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent LTB_4 receptor antagonist that inhibits the specific binding of [^{3}H]-LTB_4 to isolated human neutrophils with an IC_{50} value of 13.2 nM; inhibits the LTB_4-induced aggregation of guinea pig and human neutrophils with IC_{50} values of 74 and 100 nM, respectively

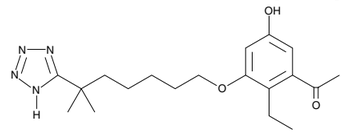
1 mg
5 mg
10 mg
25 mg



LY255283 70715

[117690-79-6]
MF: $C_{19}H_{28}N_4O_3$ **FW:** 360.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥1 year at -20°C
Summary: A competitive BLT_2 receptor antagonist; exhibits IC_{50} values of ~950 nM and >10 µM at human recombinant BLT_2 and BLT_1 receptors, respectively

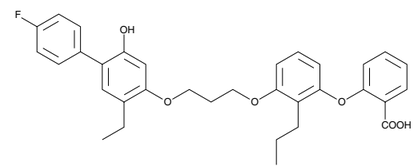
1 mg
5 mg
10 mg
25 mg



LY293111 10009768

[161172-51-6] Etalocib, VML 295
MF: $C_{33}H_{33}FO_6$ **FW:** 543.6 **Purity:** ≥98%
A crystalline solid **Stability:** ≥1 year at -20°C
Summary: A potent antagonist of the LTB_4 receptor, BLT_1, that inhibits the specific binding of radiolabeled LTB_4 to isolated human neutrophils (IC_{50} = 17.6 nM); inhibits the LTB_4-induced chemotaxis of human neutrophils (IC_{50} = 6.3 nM)

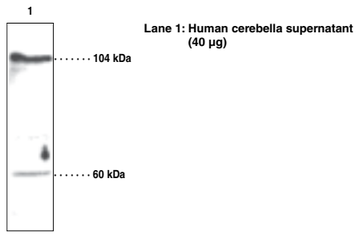
500 µg
1 mg
5 mg
10 mg



Lysophospholipase D Polyclonal Antibody 10005375

Autotaxin, ENPP2, lysoPLD
Peptide affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: rat lysoPLD amino acids 573-588 • Host: rabbit • Cross Reactivity: (+) human, mouse, and rat lysoPLD • Application(s): ICC and WB • lysoPLD was first discovered as the enzyme responsible for generating LPA from lysophosphatidylcholine (LPC). It was later revealed to be identical to an autocrine motility factor, autotaxin (ATX), which plays a role in tumor progression and metastasis.

1 ea

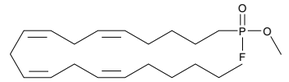


•Also Available: **Lysopholipase D Blocking Peptide** (10007193)

Methyl Arachidonyl Fluorophosphonate 70660

MAFP
MF: $C_{21}H_{36}FO_2P$ **FW:** 370.5 **Purity:** ≥98%
A solution in methyl acetate **Stability:** ≥1 year at -80°C
Summary: A selective, active-site directed, irreversible inhibitor of $cPLA_2$, and $iPLA_2$ with IC_{50} values of 0.6 and 0.5 µM, respectively; potent inhibitor of FAAH (IC_{50} = 2.5 nM); binds to the CB_1 receptor (IC_{50} = 20 nM; rat brain)

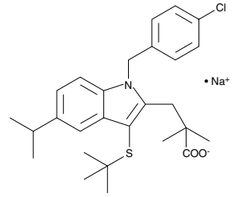
1 mg
5 mg
10 mg
50 mg



MK 886 (sodium salt) 10133

[118427-55-7]
MF: $C_{27}H_{33}ClNO_2S$ • Na **FW:** 494.1 **Purity:** ≥99%
A crystalline solid **Stability:** ≥1 year at -20°C
Summary: A potent FLAP antagonist that prevents 5-LO activation *in vivo*; inhibits LT biosynthesis in leukocytes with an IC_{50} value of 2.5 nM

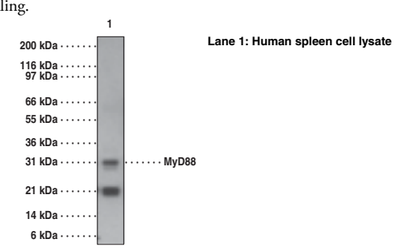
1 mg
5 mg
10 mg
25 mg



MyD88 Polyclonal Antibody 13746

Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: synthetic peptide corresponding to human MyD88 amino acid 233-248 • Host: rabbit • Cross Reactivity: (+) human, mouse, and rat MyD88 • Application(s): WB • MyD88 is a central adapter protein involved in IL-1 and TLR-mediated signaling.

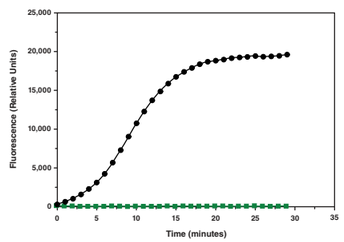
1 ea



Myeloperoxidase Chlorination Assay Kit 10006438

MPO
Stability: ≥6 months at 4°C
Summary: Cayman's MPO Chlorination Assay provides a convenient fluorescence-based method for detecting the MPO chlorination activity in both crude cell lysates and purified enzyme preparations. The assay utilizes the non-fluorescent probe, APF, which is selectively cleaved by hypochlorite to yield the highly fluorescent compound fluorescein. The kit includes an MPO-specific inhibitor for distinguishing MPO activity from MPO-independent fluroescence.

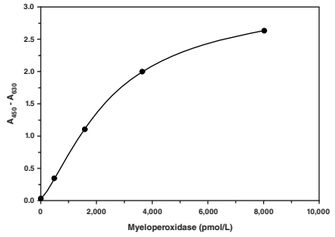
2 x 96 wells



Myeloperoxidase (human) EIA Kit 585001

MPO
Stability: ≥6 months at 4°C **Limit of Detection:** 14 pmol/L
Summary: Cayman's MPO (human) EIA is an immunometric assay which can be used to measure MPO in plasma without prior sample purification. This assay has been tested using plasma from healthy volunteers and the results were shown to be consistent with published data.

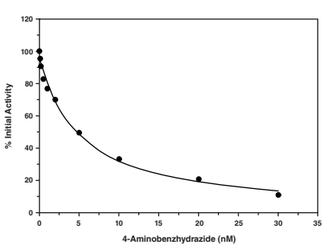
96 wells



Myeloperoxidase Inhibitor Screening Assay Kit 700170

MPO
Stability: ≥6 months at 4°C
Summary: Cayman's MPO Inhibitor Screening Assay provides fluorescence-based methods for screening inhibitors to both the chlorination and peroxidation activities of MPO. Sufficient reagents are provided for a full 96-well plate assay of each type of activity.

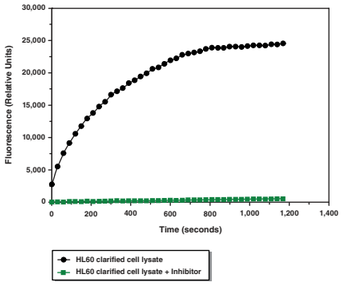
2 x 96 wells



Myeloperoxidase Peroxidation Assay Kit 700160

MPO
Stability: ≥6 months at 4°C
Summary: Cayman's MPO Peroxidation Assay provides a fluorescence-based method for detecting MPO peroxidase activity in both crude cell lysates and purified enzyme preparations. The MPO-catalyzed reaction between hydrogen peroxide and ADHP produces the highly fluorescent compound resorufin. The kit includes an MPO-specific inhibitor for distinguishing MPO activity from MPO-independent fluorescence.

2 x 96 wells



Thomas G. Brock, Ph.D.

Citrullination: Much Bigger than Watermelon

Scientists who are studying autoimmunity or rheumatoid arthritis know something that many others might not: citrullination of proteins is hugely important. This form of post-translational protein modification creates novel epitopes on common proteins, providing 'neoantigens' that are now known to be important in autoimmune disease. Citrullination can occur outside of the cell, in the cytoplasm, and in the nucleus. Because of this, it can affect such diverse processes as blood clotting, skin differentiation, and chromatin remodeling. Although the roles for this process are only beginning to be understood, citrullination has established actions in inflammatory signaling. By the end of this article, readers should not only learn some hot science to impress friends but may even have new ideas for their research ventures.

Citrulline and Watermelons

The biochemist should know about citrulline from the urea cycle, an important process for removing ammonia in animals. Citrulline is an α-amino acid that is structurally similar to arginine (Figure 1). In the urea cycle, carbamoyl phosphate is produced from ammonia, bicarbonate, and phosphate. Citrulline, synthesized from carbamoyl phosphate and ornithine by ornithine transcarbamylase, is simply an intermediate in the generation of arginine, which is then cleaved by arginase 1 to give urea and ornithine. In this cycle, citrulline is synthesized within the mitochondria and then exported to the cytoplasm for metabolism.

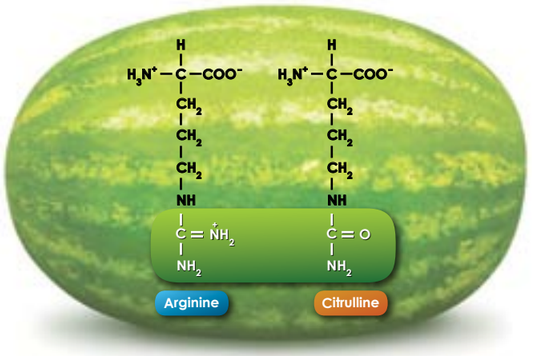


Figure 1. Watermelon (*Citrullus lanatus* L.) contains abundant arginine and citrulline as free amino acids.

The serious gardener might recognize *Citrullus lanatus* (occasionally given, mistakenly, as *C. vulgaris*) as the formal name for watermelon. These cucurbits apparently originated in southern Africa and were cultivated in the Nile Valley some 4,000 years ago. Now grown worldwide in temperate climates, watermelon is remarkably rich in citrulline and arginine as free amino acids.[1] In fact, the amino acid citrulline received its name when it was first isolated from the juice of watermelon over 80 years ago. As citrulline is a precursor of arginine and arginine can give rise to the vasoactive mediator nitric oxide, watermelon is not only tasty but also a potentially healthful treat.

Citrullination, PADs, and Rheumatoid Arthritis

Citrillunation is the enzymatic conversion of arginine to citrulline *in situ* on proteins (Figure 2). As the reaction involves the removal of an imine (double bonded nitrogen), it is catalyzed by deiminases. Known as peptidyl (protein) arginine deiminases (PAD, or PAD1), these enzymes are largely restricted to vertebrates, bacteria, and fungi. In human, rat, mouse, cow, horse, Rhesus monkey, and chimpanzee, there are 5 PAD genes, curiously numbered 1-4 and 6. In humans, each gene has a single gene product coding for a single, calcium-dependent enzyme, and each enzyme has unique substrates and functions. For example, PAD3 is found in the cytoplasm of hair follicles and keratinocytes, citrullinates filaggrin in follicles and trichohyalin in the inner root sheath, and regulates hair follicle and epidermal differentiation. Filaggrin and trichohyalin are intermediate filament-associated proteins that are involved in structurally aggregating or connecting keratin intermediate filaments. Similarly, some of the substrates of other PADs are structural proteins.[2]

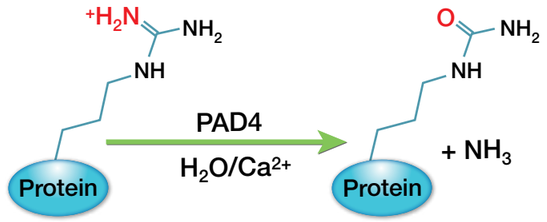


Figure 2. PADs catalyze, Ca^{2+}-dependent, imine to ketone reactions on specific peptidyl arginine side groups.

Rheumatoid arthritis (RA) has long been considered to be a systemic autoimmune disease. A major breakthrough occurred in 1998 when Schellekens and colleagues reported that many RA autoantibodies detect citrulline on peptides, that many of these were specific for RA, and that the antibodies are present early in disease.[3] Citrullination of specific proteins, including filaggrin, vimentin, fibrin, fibrinogen, α-enolase, and collagen II, produces novel epitopes that give rise to autoantibodies.[4] While anti-citrullinated protein antibodies (ACPA) are now recognized as specific biomarkers for RA, assays that use cyclic citrullinated peptide (CCP) as an artificial antigen to probe for anti-CCP have high specificity and sensitivity.[5,6] Importantly, the presence of anti-CCP antibodies can be predictive for erosive arthritis, suggesting that protein citrullination plays a role in the etiology of RA and that PAD inhibitors might be therapeutic.[7]

PAD4 is the principle citrullination enzyme in RA. It is expressed in neutrophils, eosinophils and tissue resident macrophages, but not lymphocytes or circulating monocytes. PAD4 normally has roles in cellular differentiation and the regulation of transcription of p53 and estrogen receptors. However, joint inflammation is characterized by infiltration of PAD4-bearing leukocytes. In one scenario, cellular activation, with a rise in intracellular calcium, leads to PAD4 citrullination of leukocyte vimentin, an intermediate filament involved in leukocyte attachment, migration, and cell signaling. Alternatively, widespread leukocyte necrosis resulting from release of cytotoxic compounds during degranulation results in the release of PAD4, as well as numerous cytoskeletal proteins, into the calcium-rich inflammatory milieu, resulting in indiscriminate citrullination of multiple targets. In either case, the stage is set for the development of autoantibodies. One question remains: why doesn't this happen in more inflammatory settings?

Citrullination Within the Nucleus

As mentioned above, each of the five PAD enzymes appears to have distinct substrates and roles (see Table 1). For example, while PAD1 and PAD3 are both associated with epithelium and can contribute to keratinocyte differentiation, PAD1 is primarily involved in maintaining cutaneous barrier function and PAD3 has a central role in follicle development. Of all the PADs, PAD4 appears to be unique in its ability to enter the nucleus. As a result, PAD4 can citrullinate nuclear substrates, including the histones H2A, H3, and H4, as well as the histone acetyltransferase p300. While the actions and implications of PAD4 in the nucleus are still poorly understood, interesting aspects have been revealed. First, deimination interplays with methylation of arginine residues: PAD4 can remove monomethyl groups from arginine residues through a demethyliminase activity, reversing the actions of protein arginine methyltransferases (PRMT) (Figure 3).[8] PAD4 cannot, however, act on dimethylated residues. Similarly, deimination by PAD4 prevents arginine methylation.[9] Thus, PAD4 can block or reverse some of the actions of PRMT.

Table 1. PAD enzymes, their substrates, and their cellular/tissue distributions

Enzyme	Substrates	Cellular/tissue distributions
PAD1	keratin K1, filaggrin	epidermis, uterus, keratinocytes
PAD2	vimentin, myelin basic protein, glial fibrillary acidic protein	skeletal muscle, brain, pancreas, glial cells, macrophages, bone marrow, muscle, breast, colon, embryo, eye, kidney, epidermis, uterus, thymus
PAD3	Trichohyalin, filaggrin	hair follicles, keratinocytes
PAD4	H2A, H3, H4, vimentin, nucleophosmin, p300, PAD4, 40S ribosomal protein S2, antithrombin	eosinophils, neutrophils
PAD6	unknown	egg, ovary, early embryo, thymus, oocyte

PAD4 also interplays with protein acetylation/deacetylation. In order for some nuclear receptors to activate transcription in the presence of ligand, they must first recruit a p160 coactivator, which in turn binds the histone acetyltransferase p300. This allows acetylation that is necessary for chromatin remodeling, histone eviction, or transcriptional coactivation. The binding of p300 to the coactivator p160 is inhibited by methylation of Arg^{2142} on p300 by CARM1 (PRMT4), preventing transcription.[10] This methylation mark is removed by PAD4, enhancing the p160-p300 interaction and transcription. In addition, PAD4 directly associates with histone deacetylase 1 (HDAC1), positioning the two proteins and their activities together in specific protein complexes.[11] On the pS2 promoter, which is driven cyclically by the estrogen receptor alpha (ERα), PAD4 and HDAC1 bind and then release together in a periodic manner, with corresponding increases and decreases in citrullination and deacetylation of H3. The association of PAD4 and HDAC1 on pS2 produces a reversible, repressive chromatin environment.[11,12]

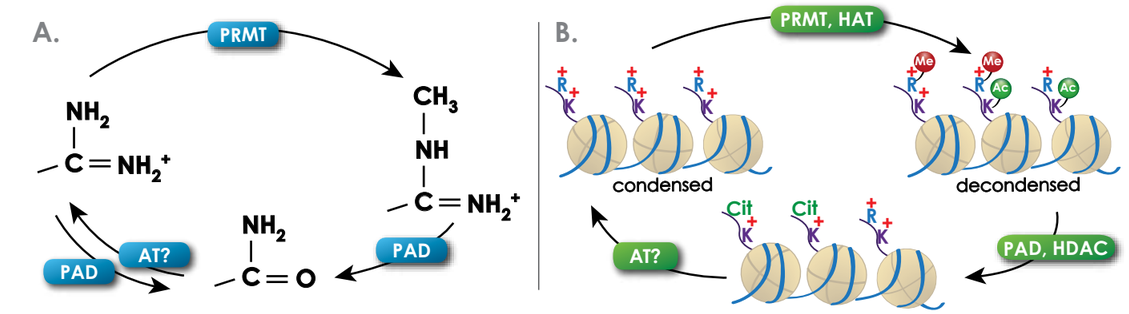


Figure 3. PADs demethylate mono-methyated arginine residues. (A) PADs produce citrullinated side chains on either normal arginine or arginine that has been mono-methylated by PRMTs. Aminotransferases (AT) may convert citrullinated chains to iminated chains. (B) PRMTs work with HATs to decondense chromatin. PADs and HDACs initiate the return of chromatin to a condensed form by citrullinating mono-methylated arginine and deacetylating lysine residues on histone tails.

Cancer and Nets

The tumor suppressor protein p53 regulates the expression of various target genes, whose products in turn modulate cell growth and apoptosis. PAD4 and HDAC2 interact with p53 *via* distinct domains, resulting in their co-localization at p53-regulated promoters and suppression of transcription.[13,14] The PAD4 inhibitor Cl-amidine and the HDAC inhibitor SAHA additively induce gene expression. PAD4's role as a transcription co-repressor for p53 may help explain the role of PAD4 in cancer: the deiminase is overexpressed in cancers of the breast, lung, liver, esophagus, colon, kidney, ovaries, endometrium, uterine, and bladder.[15] The PAD4 inhibitors F- and Cl-amidine display cytotoxic effects towards cancerous cell lines but not against non-cancerous lines.[16] This suggests that PAD4 inhibitors would be useful for treating certain cancers, as well as RA.

On a different front, citrullination by PAD4 plays a role in the immune response to bacteria. In addition to their vast granulocytic armamentarium, neutrophils unleash highly decondensed chromatin structures, called neutrophil extracellular traps (NETs) to trap and kill pathogenic bacteria.[17] Impaired NET formation predisposes individuals to bacterial infection. Uncontrolled hypercitrullination of histones by PAD4 mediates chromatin decondensation.[18] PAD4 deficient neutrophils cannot make NETs and $PAD4^{-/-}$ mice are more susceptible to bacterial infection than $PAD4^{+/+}$ mice.[19] Taken together, these results suggest that the systemic use of PAD4 inhibitors would compromise immune defense against infection.

References

1. Tedesco, T.A., Benford, S.A., Foster, R.C., *et al. Pediatrics* **73(6)**, 879 (1984).
2. Jones, J.E., Causey, C.P., Knuckley, B., *et al. Curr. Opin. Drug Discov. Devel.* **12(5)**, 616-627 (2009).
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NF-κB (p50) (human recombinant) 10009818

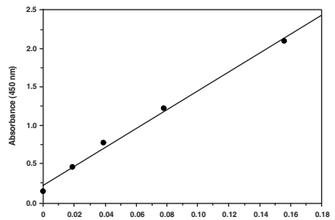
NF-κB1
M_r: 74.5 kDa **Purity:** ≥75%
Supplied in: PBS, pH 7.4, containing 5 mM DTT and 20% glycerol
Summary: Recombinant GST-tagged protein expressed in *E. coli* • As part of a dimer, this transcription factors binds with p65 to form NF-κB, which is responsible for regulating the expression of inflammatory cytokines, chemokines, immunoreceptors, and cell adhesion molecules

5 µg
10 µg
25 µg

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

Stability: ≥6 months at -80°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) and will not cross-react with NF-κB (p65).

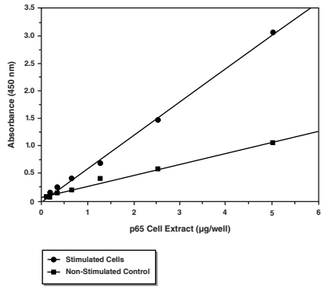
96 wells



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

Stability: ≥6 months at -80°C
Summary: Cayman's NF-κB (human p50/p65) Combo Transcription Factor Assay is a non-radioactive, sensitive method for detecting p50 and p65 transcription factor DNA binding activity in nuclear extracts.

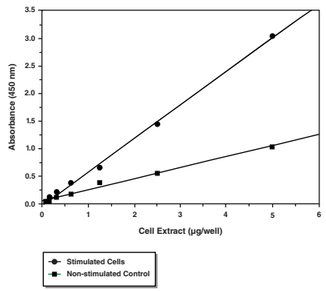
96 wells



NF-κB (p65) Transcription Factor Assay Kit 10007889

Stability: ≥6 months at -80°C
Summary: Cayman's NF-κB (p65) Transcription Factor Assay detects human NF-κB (p65). It will not cross-react with NF-κB (p50).

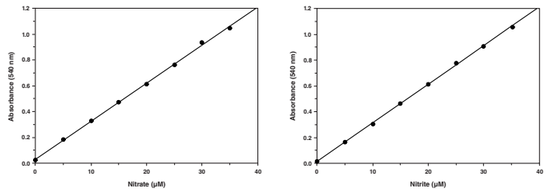
96 wells



Nitrate/Nitrite Colorimetric Assay Kit 780001

Nitric Oxide Metabolite Detection Kit
Stability: ≥1 year at -20°C
Summary: Cayman's Nitrate/Nitrite Assay provides an accurate and convenient method for measurement of total nitrate/nitrite concentrations. This kit can be used to measure nitrate and nitrite in plasma, serum, urine, tissue culture media, and tissue homogenates.

2 x 96 wells

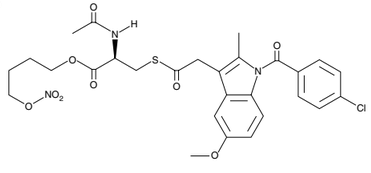


• Also Available: **Nitrate/Nitrite Colorimetric Assay Kit (LDH method)** (760871)
Nitrate/Nitrite Fluorometric Assay Kit (780051)

NO-Indomethacin 10005705

[301838-28-8] NCX 2121
MF: $C_{28}H_{30}ClN_3O_9S$ **FW:** 619.1 **Purity:** ≥98%
A solution in methyl acetate **Stability:** ≥1 year at -20°C
Summary: A hybrid molecule of indomethacin and an NO donor which combines the anti-inflammatory properties of an NSAID with the gastrointestinal protective effects of NO

1 mg
5 mg
10 mg
50 mg



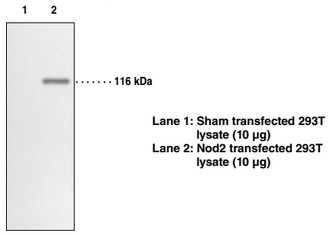
IκB, IKK, and NF-κB Antibodies

Antibody	Antigen	Cross Reactivity	Application	Supplied As
IκBα Monoclonal Antibody (Clone 6A920) Item No. 13918	Amino acids 32-291 from human IκBα **Host:** mouse	(+) human and mouse IκBα	FC (intracellular) - 0.5-1 µg/10^6 cells IHC (paraffin-embedded sections) IP - 1 µg/ml WB - 1-2 µg/ml	Protein G-purified IgG
IκBα Monoclonal Antibody - biotin (Clone 6A920) Item No. 13922	Amino acids 32-291 from human IκBα **Host:** mouse	(+) human and mouse IκBα	ELISA	Biotinylated, protein G-purified IgG
IκBα (cleavage specific) Monoclonal Antibody (Clone 5D1623) Item No. 13925	Caspase-3 mediated cleavage site of IκBα **Host:** mouse	(+) human IκBα	WB - 1 µg/ml	Protein G-purified IgG
IκBα (Phospho-Ser$^{32/36}$) Monoclonal Antibody (Clone 39A1413) Item No. 13923	Amino acids 32 and 36 from human IκBα **Host:** mouse	(+) bovine, canine, human, mouse, pocine, and rat IκBα	IP - 1-2 µg/ml WB - 1-2 µg/ml	Protein G-purified IgG
IκBα (Phospho-Ser$^{32/36}$) Monoclonal Antibody - biotin (Clone 39A1413) Item No. 13924	Amino acids 32 and 36 from human IκBα **Host:** mouse	(+) bovine, canine, human, mouse, pocine, and rat IκBα	ELISA	Biotinylated, protein G-purified IgG
IκBα Polyclonal Antibody Item No. 13921	Human IκBα **Host:** rabbit	(+) human IκBα (-) mouse IκBα	WB - 0.5-2 µg/ml	Protein G-purified IgG
IκBα Polyclonal Antibody (aa 34-48) Item No. 13919	Amino acids 34-48 from human IκBα **Host:** rabbit	(+) human IκBα	WB - 1-3 µg/ml	Protein G-purified IgG
IκBζ Polyclonal Antibody Item No. 13926	Amino acids 684-699 and 285-298 from mouse IκBζ **Host:** rabbit	(+) mouse IκBζ	WB - 1-3 µg/ml	Protein G-purified IgG
IKKα Monoclonal Antibody (Clone 14A231) Item No. 13927	IKKα **Host:** rabbit	(+) human, monkey, and mouse IKKα	FC (intracellular) - 0.25-0.5 µg/10^6 cells IHC (paraffin-embedded sections) - 5 µg/ml IP - 1-2 µg/ml WB - 1 µg/ml	Protein G-purified IgG
IKKε Monoclonal Antibody (Clone 72B587) Item No. 13929	Amino acids 175-188 from human IKKε **Host:** rabbit	(+) human, mouse, and rat IKKε	FC (intracellular) - 0.1-0.5 µg/ml WB - 1-3 µg/ml	Protein G-purified IgG
IKKε Polyclonal Antibody Item No. 13928	Amino acids 175-188, 526-540, and 567-580 from human IKKε **Host:** rabbit	(+) human IKKε	WB - 2 µg/ml	Protein G-purified IgG
IKKγ Monoclonal Antibody (Clone 46B844) Item No. 13930	Full-length human IKKγ **Host:** mouse	(+) human IKKγ	FC (intracellular) - 0.1-0.5 µg/ml WB - 2 µg/ml	Protein G-purified IgG
IKKγ Monoclonal Antibody (Clone 72C627) Item No. 13931	Full-length human IKKγ **Host:** mouse	(+) human and mouse IKKγ	WB - 2 µg/ml	Protein G-purified IgG
NF-κB (p50) Monoclonal Antibody (Clone 2J10D7) Item No. 13755	Amino acids 150-200 from mouse NF-κB (p50) **Host:** mouse	(+) human NF-κB (p50)	IHC - 5 µg/ml WB - 2-5 µg/ml	Protein G-purified IgG
NF-κB (p50) Polyclonal Antibody Item No. 13754	Amino acids 150-200 from mouse NF-κB **Host:** rabbit	(+) Chimpanzee, human, and Rhesus monkey NF-κB (p50)	WB - 0.5-2 µg/ml	Protein G-purified IgG
NF-κB (p65) Monoclonal Antibody (Clone 112A1021) Item No. 13752	Amino acids 526-539 from human NF-κB (p65) **Host:** mouse	(+) human, mouse, and rat NF-κB (p65)	FC - 0.25-0.5 µg/10^6 cells WB - 2-5 µg/ml	Protein G-purified IgG
NF-κB (p65) Monoclonal Antibody - biotin (Clone 112A1021) Item No. 13756	Amino acids 526-539 from human NF-κB (p65) **Host:** mouse	(+) human, mouse, and rat NF-κB (p65)	ELISA	Protein G-purified IgG
NF-κB (p65) Polyclonal Antibody (aa 2-17) Item No. 13757	Amino acids 2-17 from human NF-κB (p65) **Host:** rabbit	(+) Chimpanzee, human, and Rhesus monkey NF-κB (p65)	WB - 0.5-2 µg/ml	Protein G-purified IgG
NF-κB (p65) Polyclonal Antibody (aa 538-546) Item No. 13753	Amino acids 538-546 from human NF-κB (p65) **Host:** mouse	(+) human, mouse, and rat NF-κB (p65)	WB - 1:500-1:1,000	Protein G-purified IgG
NF-κB (p65) NLS Polyclonal Antibody Item No. 13751	Portion of NF-κB (p65) NLS **Host:** rabbit	(+) bovine, chimpanzee, gorilla, equine, human, monkey, and mouse NF-κB (p65)	ICC - 5 µg/ml WB - 1-3 µg/ml	Protein G-purified IgG

Nod2 Monoclonal Antibody (Clone 2D9) 10004942

Protein-A purified IgG1κ **Stability:** ≥1 year at 4°C
Summary: Antigen: human recombinant Nod2 amino acids 28-301 • Host: mouse, clone 2D9 • Cross Reactivity: (+) human Nod2 • Application(s): IHC and WB • Nod2 is a member of a protein family of apoptosis regulators which includes Apaf-1 and Nod1/CARD4. Nod1/CARD4 is broadly expressed, however Nod2 expression is limited to monocytes. Both Nod1 and Nod2 act as intracellular receptors for LPS leading to activation of NF-κB. A frameshift mutation in the Nod2 gene confers susceptibility to Crohn's disease, possibly by causing truncation of the 10th LRR resulting in a protein that is unresponsive to LPS.

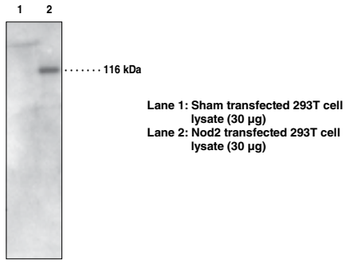
1 ea



Nod2 Polyclonal Antibody 160777

100 µg Lyophilized IgG **Stability:** ≥2 years at -20°C
Summary: Antigen: human recombinant Nod2 amino acids 28-301 • Host: rabbit • Cross Reactivity: (+) Nod2 transfected 293T cell lysate; (-) sham transfected 293T cell lysate • Application(s): IP and WB • Nod2 is a member of a protein family of apoptosis regulators which includes Apaf-1 and Nod1/CARD4. Nod1/CARD4 is broadly expressed, however NOD2 expression is limited to monocytes. Both Nod1 and Nod2 act as intracellular receptors for LPS leading to activation of NF-κB. A frameshift mutation in the Nod2 gene confers susceptibility to Crohn's disease, possibly by causing truncation of the 10th LRR resulting in a protein that is unresponsive to LPS.

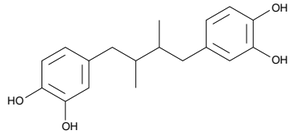
500 µl



Nordihydroguaiaretic Acid 70300

[500-38-9] NDGA
MF: $C_{18}H_{22}O_4$ **FW:** 302.4 **Purity:** ≥95%
A crystalline solid **Stability:** ≥1 year at -20°C
Summary: A non-selective LO inhibitor; inhibits A23187-induced CysLT biosynthesis in rat peritoneal cells with an IC_{50} value of 5-7 µM; exhibits IC_{50} values of 3.0-5.0 µM for inhibition of human platelet 12-LO and 0.91 µM for rabbit reticulocyte 15-LO

500 mg
1 g
5 g
25 g



NOS Activity Assay Kit 781001

Stability: ≥1 year at -80°C
Summary: The NOS Activity Assay measures NOS activity by monitoring the conversion of radiolabeled arginine to citrulline. This assay is simple, sensitive, and specific for NOS activity and can be used with both crude and purified enzyme preparations. The kit includes sufficient materials and reagents for 50 total reactions. Radiolabeled arginine and NADPH are not included with the kit.

1 ea

iNOS (murine recombinant) 60864

NOS II
MF: Homodimer **M_r:** 130 kDa/subunit **Purity:** cell lysate 100,000 x g supernatant
Supplied in: 50 mM HEPES, pH 7.4, containing 30% glycerol and 8 µM BH_4
Summary: Recombinant enzyme expressed in *E. coli* • A soluble enzyme induced by LPS and cytokines that is responsible for the biosynthesis of NO from L-arginine; one unit of enzyme produces 1 nmol of NO per minute at 37°C in 50 mM HEPES, pH 7.4, containing 1 mM arginine, 1 mM magnesium acetate, 5 µM oxyhemoglobin, 0.1 mM NADPH, 12 µM tetrahydrobiopterin, and 170 µM DTT

50 units
100 units
250 units

iNOS Polyclonal Antibody 160862

NOS II
Protein A-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: purified enzyme from mouse macrophages (RAW 264.7 cells) • Host: rabbit • Cross Reactivity: (+) iNOS from most mammalian species and nNOS (~5%); (-) eNOS • Application(s): ICC, IP, and WB • iNOS is a soluble enzyme found in a variety of tissues including macrophages, hepatocytes, vascular smooth muscle cells, and chondrocytes. iNOS expression is increased by a variety of factors including LPS, IFN-γ, IL-1β, and TNF-α.

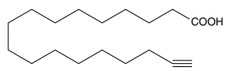
500 µl

•Also Available: **iNOS Electrophoresis Standard** (360862)

17-Octadecynoic Acid 90270

[34450-18-5] 17-ODA, ODYA
MF: $C_{18}H_{32}O_2$ **FW:** 280.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥1 year at -20°C
Summary: A suicide inhibitor of LTB_4 20-hydroxylase and renal CYP450 ω-hydroxylase

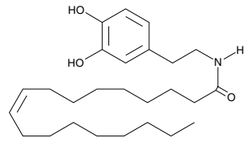
1 mg
5 mg
10 mg
100 mg



N-Oleoyl Dopamine 10115

[105955-11-1] ODA
MF: $C_{26}H_{43}NO_3$ **FW:** 417.6 **Purity:** ≥98%
A solution in ethanol **Stability:** ≥1 year at -20°C
Summary: A selective, endogenous VR_1 agonist; binds to the human recombinant VR_1 with a K_i value of 36 nM; potent inhibitor of 5-LO from RBL-1 cells (IC_{50} = 7.5 nM)

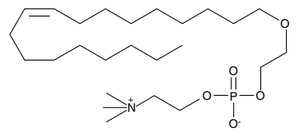
5 mg
10 mg
50 mg
100 mg



Oleyloxyethyl Phosphorylcholine 70560

[84601-19-4]
MF: $C_{25}H_{52}NO_5P$ **FW:** 477.7 **Purity:** ≥98%
A solution in ethanol **Stability:** ≥2 years at -20°C
Summary: An inhibitor of PLA_2 (IC_{50} = 6.2 µM for porcine pancreatic PLA_2)

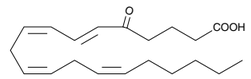
1 mg
5 mg
10 mg
50 mg



5-OxoETE 34250

[106154-18-1] 5-KETE
MF: $C_{20}H_{30}O_3$ **FW:** 318.5 **Purity:** ≥95%
A solution in ethanol **Stability:** ≥1 year at -80°C
Summary: A polyunsaturated keto acid formed by the oxidation of 5-HETE in neutrophils by a specific dehydrogenase; stimulates the increase in cytosolic calcium levels in neutrophils (EC_{50} = 2 nM) and stimulates the migration and degranulation of eosinophils *via* a specific GPCR

25 µg
50 µg
100 µg
250 µg



•Also Available: **5-OxoETE-d_7** (334250)
5-OxoETE Lipid Maps MS Standard (10007244)

5-OxoETE Receptor Polyclonal Antibody 100025

R527, TG1019
Peptide affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human 5-OxoETE receptor C-terminal amino acids 408-423 • Host: rabbit • Cross Reactivity: (+) human, mouse, rat, porcine, and Cos-7 (African green monkey) 5-OxoETE receptors • Application(s): ICC and WB • The 5-OxoETE receptor is a GPCR that mediates the action of 5-OxoETE, a potent stimulator of chemotaxis for eosinophils and neutrophils. The 5-OxoETE receptor couples to $G_{i/o}$ to inhibit cyclic AMP production and to mobilize intracellular calcium.

500 µl

•Also Available: **5-OxoETE Receptor Blocking Peptide** (10006618)

PAD4 (human recombinant) 10784

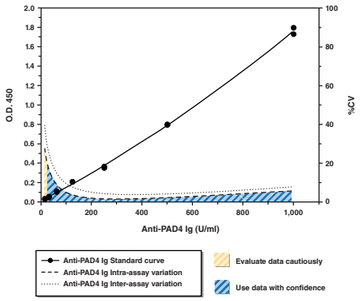
Peptidylarginine Deiminase 4, Protein-Arginine Deiminase 1
M_r: 76.4 kDa **Purity:** ≥95%
Supplied in: 20 mM Tris-HCl, pH 7.6, containing 100 mM sodium chloride, 1 mM DTT, and 20% glycerol
Summary: PAD4 is a homodimer that functions as a transcriptional coregulator to catalyze the conversion of specific 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. Recombinant N-terminal hexahistadine-tagged protein expressed in *E. coli*

50 µg
100 µg
250 µg

PAD4 Autoantibody EIA Kit 500930

Peptidylarginine Deiminase 4 Autoantibody, Protein Arginine Deiminase 4
Stability: ≥6 months at -20°C
Summary: PAD4, is a guanidino-modifying enzyme which catalyzes the conversion of specific arginine residues to citrulline in a calcium-dependent manner. PAD4 activity is increased in rheumatoid arthritis (RA), producing citrulline-containing proteins (CCP) that induce the formation of arthritogenic autoantibodies. In addition to anti-CCP autoantibodies, 23-45% of RA patients also produce autoantibodies specific for the PAD4 enzyme itself. Cayman's PAD4 Autoantibody EIA Kit is an immunometric assay which can be used to measure anti-PAD4 autoantibodies of any isotype (IgM, IgG, and IgA) in human plasma and serum without prior sample purification. Affinity-purified anti-PAD4 antibody isolated from the plasma of a patient with RA is used as the standard. One unit is approximately equal to 1 ng of anti-PAD4 Ig protein. The standard curve spans the range of 0-2,000 U/ml, with an limit of quantification (LOQ) of 62.5 U/ml.

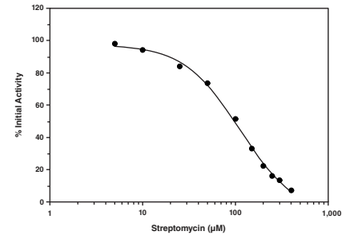
96 wells



PAD4 Inhibitor Screening Assay Kit 700560

Peptidylarginine Deiminase 4, Protein Arginine Deiminase 4
Stability: ≥6 months at -80°C
Summary: PAD4 is a guanidino-modifying enzyme that functions as a transcriptional coregulator catalyzing the conversion of specific arginine residues to citrulline. Substrates for PAD4 include histones H2A, H3, and H4. PAD4 autocitrullinates itself at several sites, inhibiting its enzymatic activity. PAD4 activity is increased in rheumatoid arthritis, producing an abundance of citrulline-containing proteins that generate an immune response resulting in production of autoantibodies that ultimately attack the host tissues. PAD4 has also been implicated in several other diseases including multiple sclerosis, Alzheimer's disease, glaucoma, and cancer. Cayman's PAD4 Inhibitor Screening Assay provides a convenient, fluorescence-based method for screening human PAD4 inhibitors.

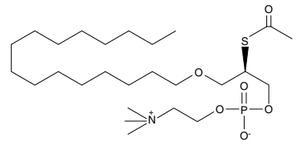
96 wells



2-thio-PAF 60945

[96801-55-7]
MF: $C_{26}H_{54}NO_6PS$ **FW:** 539.8 **Purity:** ≥98%
A solution in ethanol **Stability:** ≥1 year at -80°C
Summary: A PAF receptor agonist with potency comparable to PAF C-18 and PAF C-16; chromogenic substrate used in Cayman's PAF-AH Assay Kit (Item No. 760901)

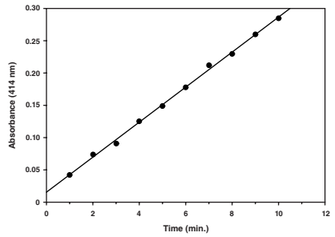
5 mg
10 mg
25 mg
50 mg



PAF Acetylhydrolase Assay Kit 760901

Lp-PLA$_2$, PAF-AH
Stability: ≥1 year at -20°C
Summary: PAF-AH catalyzes the hydrolysis of the potent biologically-active phospholipid PAF, generating inactive lyso-PAF. Cayman's PAF-AH Assay provides an accurate and convenient method for measurement of PAF-AH activity. The assay uses 2-thio PAF which serves as a substrate for PAF-AH. Upon hydrolysis of the acetyl thioester bond at the *sn*-2 position by PAF-AH, free thiols are detected using DTNB (Ellman's reagent).

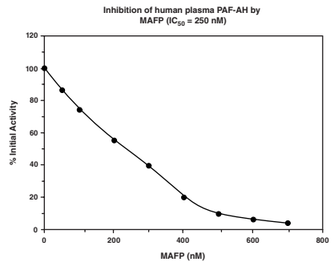
96 wells



PAF Acetylhydrolase Inhibitor Screening Assay Kit 10004380

Lp-PLA$_2$, PAF-AH
Stability: ≥1 year at -20°C
Summary: Cayman's PAF-AH Inhibitor Screening Assay uses 2-thio PAF as a substrate for PAF-AH. Upon hydrolysis of the acetyl thioester bond at the *sn*-2 position by PAF-AH, free thiols are detected using DTNB (Ellman's reagent).

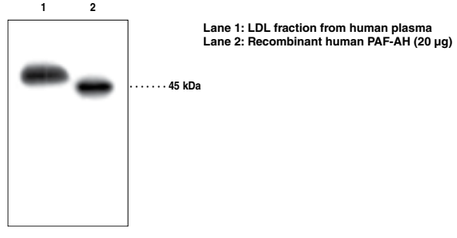
96 wells



PAF Acetylhydrolase (human) Polyclonal Antibody 160603

Lp-PLA$_2$, PAF-AH
Peptide affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human PAF-AH C-terminal amino acids 420-441 • Host: rabbit • Cross Reactivity: (+) human plasma PAF-AH; (-) mouse, guinea pig, canine, and chicken PAF-AH • Application(s): WB • PAF-AH converts PAF to the biologically inactive lyso-PAF. Plasma PAF-AH is highly selective for phospholipids with very short acyl groups at the *sn*-2 position and is associated with lipoproteins. It has been linked to atherosclerosis and may be a positive risk factor for coronary heart disease in humans.

500 µl



•Also Available: **PAF Acetylhydrolase (human) Blocking Peptide** (360603)
PAF Acetylhydrolase (human recombinant) (10279)

PAF Receptor (human) Monoclonal Antibody (11A4, Clone 21) 160600

Protein-A purified IgG$_{2a}$ IgG **Stability:** ≥18 months at 4°C
Summary: Antigen: human PAF receptor amino acids 260-269 • Host: mouse, clone 11A4 (clone 21) • Isotype: IgG$_{2a}$ • Cross Reactivity: (+) human, bovine, and porcine PAF receptors • Application(s): FC and ICC; (-) WB • PAF is a biologically active phospholipid whose biological effects include activation of platelets, neutrophils, monocytes, and macrophages. PAF increases vascular permeability, decreases cardiac output, induces hypotension, and stimulates uterine contraction.

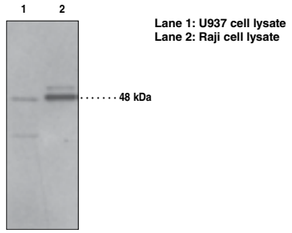
1 ea

•Also Available: **PAF Acetylhydrolase (human) Blocking Peptide (Monoclonal)** (360600)

PAF Receptor (human) Polyclonal Antibody 160602

Peptide affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human PAF receptor amino acids 1-17 • Host: rabbit • Cross Reactivity: (+) human, mouse, rat, and porcine PAF receptors • Application(s): FC, ICC, and WB • PAF is a biologically active phospholipid whose biological effects include activation of platelets, neutrophils, monocytes, and macrophages. PAF increases vascular permeability, decreases cardiac output, induces hypotension, and stimulates uterine contraction.

1 ea

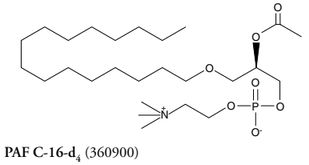


•Also Available: **PAF Acetylhydrolase (human) Blocking Peptide (Polyclonal)** (160604)

PAF C-16 60900

[74389-68-7]
MF: $C_{26}H_{54}NO_7P$ **FW:** 523.7 **Purity:** ≥98%
A lyophilized powder **Stability:** ≥1 year at -20°C
Summary: A naturally occurring phospholipid involved in pathological processes such as necrotizing enterocolitis, inflammation, asthma, and allergy

5 mg
10 mg
50 mg
100 mg

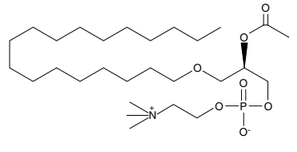


•Also Available: **PAF C-16-d$_4$** (360900)

PAF C-18 60910

[74389-69-8]
MF: $C_{28}H_{58}NO_7P$ **FW:** 551.7 **Purity:** ≥97%
A solution in ethanol **Stability:** ≥2 years at -20°C
Summary: A naturally occurring phospholipid involved in pathological processes such as necrotizing enterocolitis, inflammation, asthma, and allergy

5 mg
10 mg
50 mg
100 mg

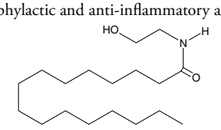


•Also Available: **PAF C-18-d$_4$** (10010229)

Palmitoyl Ethanolamide 90350

[544-31-0] Palmidrol, PEA
MF: $C_{18}H_{37}NO_2$ **FW:** 299.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An endogenous CB found in egg yolk, brain, liver, and other mammalian tissues; exhibits anti-anaphylactic and anti-inflammatory activity *in vitro*

5 mg
10 mg
50 mg
100 mg

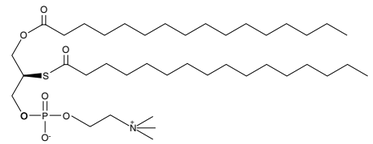


•Also Available: **Palmitoyl Ethanolamide-d$_4$** (10007824)
Palmitoyl Ethanolamide-d$_4$ (9000551)
Palmitoyl Ethanolamide-d$_5$ (9000573)

Palmitoyl thio-PC 10010521

[113881-60-0]
MF: $C_{40}H_{80}NO_7PS$ **FW:** 750.1 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A chromogenic PLA$_2$ substrate that contains a palmitoyl thioester at the *sn*-2 position of the glycerol backbone

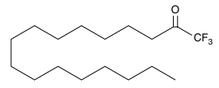
1 mg
5 mg
10 mg
50 mg



Palmityl Trifluoromethyl Ketone 62650

[141022-99-3] Pentadeca Trifluoromethyl Ketone, PTK
MF: $C_{17}H_{31}F_3O$ **FW:** 308.4 **Purity:** ≥98%
A solution in ethanol **Stability:** ≥2 years at -20°C
Summary: An inhibitor of iPLA$_2$ (IC_{50} = 3.8 µM) and also of cPLA$_2$ with an IC_{50} value almost identical to that of ATK

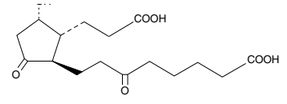
1 mg
5 mg
10 mg
25 mg



tetranor-PGDM 12850

[133161-96-3] tetranor-Prostaglandin D Metabolite
MF: $C_{16}H_{24}O_7$ **FW:** 328.4 **Purity:** ≥98%
A solution in methyl acetate **Stability:** ≥1 year at -80°C
Summary: A major metabolite of PGD$_2$ found in human and mouse urine at levels of approximately 1.5 and 8.1 ng/mg creatinine, respectively

25 µg
50 µg
100 µg
500 µg

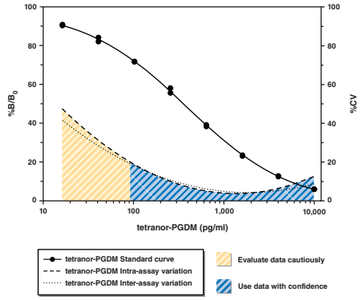


•Also Available: **tetranor-PGDM-d$_6$** (10009039)

tetranor-PGDM EIA Kit 501001

tetranor-Prostaglandin D Metabolite ELISA Kit
Stability: ≥1 year at -20°C
Sensitivity: 50% B/B$_0$: 30 pg/ml • 80% B/B$_0$: 55pg/ml
Summary: tetranor-PGDM is a major metabolite of PGD$_2$ found in human and mouse urine with normal levels of 1.5 ng/mg creatinine and 8.1 ng/mg creatinine respectively. Cayman's tetranor-PGDM EIA is a competitive assay that can be used for quantification of tetranor-PGDM in urine.

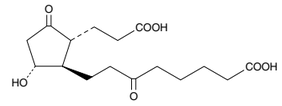
96 strip/solid wells
480 strip/solid wells



tetranor-PGEM 14840

[24769-56-0] tetranor-Prostaglandin E Metabolite
MF: $C_{16}H_{24}O_7$ **FW:** 328.4 **Purity:** ≥98%
A solution in methyl acetate **Stability:** ≥6 months at -80°C
Summary: Major urinary metabolite of PGE$_1$ and PGE$_2$ that is used as a marker of PGE$_2$ biosynthesis

25 µg
50 µg
100 µg
500 µg

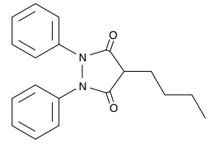


•Also Available: **tetranor-PGEM-d$_6$** (314840)
tetranor-PGEM Lipid Maps MS Standard (10007216)

Phenylbutazone 70400

[50-33-9]
MF: $C_{19}H_{20}N_2O_2$ **FW:** 308.4 **Purity:** ≥99%
A crystalline solid **Stability:** ≥2 years at room temperature
Summary: A nonsteroidal anti-inflammatory drug that acts as an efficient reducing cofactor for the peroxidase activity of COX

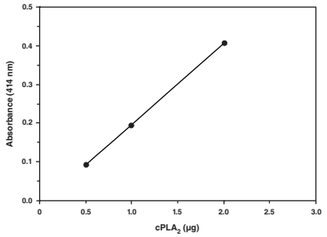
1 g
50 g



$cPLA_2$ Assay Kit 765021

Calcium-dependent cytosolic PLA_2, PLA_2 Type IV
Stability: ≥1 year at -20°C
Summary: Arachidonoyl thio-PC is a substrate for $cPLA_2$ by virtue of the presence of arachidonic acid at the *sn*-2 position of the glycerophospholipid. Hydrolysis of the arachidonoyl thioester bond at the *sn*-2 position by PLA_2 releases a free thiol which can be detected by DTNB. This assay can be used to determine the activity of $cPLA_2$ in purified preparations, cell cultures, or tissue homogenates that are known to contain only $cPLA_2$. Use of this assay with preparations containing more than one type of PLA_2 will result in the measurement of total PLA_2 activity rather than $cPLA_2$ alone. Isozyme-specific $cPLA_2$ activity can be measured by excluding $sPLA_2$ or inhibiting $iPLA_2$ activities in the assay.

96 wells



$iPLA_2$ (Type VI) Polyclonal Antibody 160507

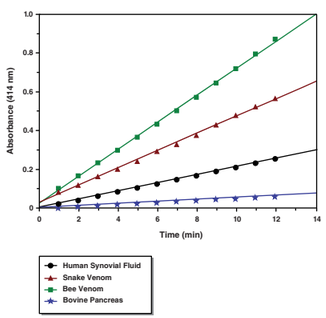
Calcium-independent Phospholipase A_2
Lyophilized antibody **Stability:** ≥2 years at -20°C
Summary: Antigen: hamster $iPLA_2$ amino acids 557-576 • Host: rabbit • Cross Reactivity: (+) human, mouse, bovine, hamster, and rat $iPLA_2$; (-) $cPLA_2$ and $sPLA_2$ • Application(s): WB • $iPLA_2$ is one of the well-characterized isoforms of the PLA_2 enzyme family. $iPLA_2$ is the major isoform of PLA_2 found in A-10 smooth muscle cells.The enzyme has a molecular weight of about 80-85 kDa and is classified as a type VI PLA_2.

500 µl

$sPLA_2$ Assay Kit 765001

Stability: ≥1 year at -20°C
Summary: Cayman's $sPLA_2$ Assay provides an accurate and convenient method for measurement of $sPLA_2$ activity. This assay uses the 1,2-dithio analog of diheptanoyl phosphatidylcholine which serves as a substrate for most PLA_2s with the exception of $cPLA_2$. Upon hydrolysis of the thioester bond at the *sn*-2 position by PLA_2, free thiols are detected using DTNB.

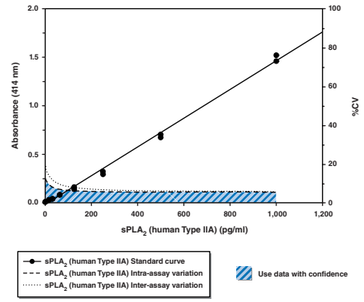
96 wells



$sPLA_2$ (human Type IIA) EIA Kit 585000

Stability: ≥1 year at -20°C **Limit of Detection:** 15 pg/ml
Summary: Cayman's $sPLA_2$ EIA Kit is an immunometric (*i.e.,* "sandwich") assay that can be used for the quantification of $sPLA_2$ in plasma, synovial fluid, and other sample matrices.

96 wells
480 wells

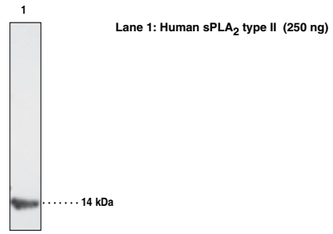


•Also Available: **$sPLA_2$ (human Type IIA) Affinity Sorbent** (485009)

$sPLA_2$ (human Type IIA) Monoclonal Antibody (Clone SCACC353) 160500

Lyophilized IgG **Stability:** ≥2 years at -20°C
Summary: Antigen: human recombinant $sPLA_2$ (type IIA) • Host: mouse, clone SCACC353 • Isotype: IgG_1 • Cross Reactivity: (+) human $sPLA_2$ (Type IIA); (-) bee venom $sPLA_2$ (Type III) and human $sPLA_2$ (Type V) • Application(s): IP and WB • PLA_2 catalyzes the hydrolysis of phospholipids at the *sn*-2 position yielding a free fatty acid and a lysophospholipid. Human synovial $sPLA_2$ is a secreted, 14 kDa protein which is dependent on Ca^{2+} for optimal activity.

1 ea



$sPLA_2$ (human Type IIA) Polyclonal Antiserum 160502

Lyophilized antiserum **Stability:** ≥2 years at -20°C
Summary: Antigen: human recombinant $sPLA_2$ (Type IIA) • Host: rabbit • Cross Reactivity: (+) human (Type IIA) and rat cardiocyte $sPLA_2$; (-) human $sPLA_2$ (Type V), bee venom (Type III), snake venom *(Naja naja)*, bovine pancreas, and porcine pancreas $sPLA_2$ • Application(s): IHC, IP, and WB • $sPLA_2$ catalyzes the hydrolysis of phospholipids at the *sn*-2 position yielding a free fatty acid and a lysophospholipid.

500 µl

$sPLA_2$ (human recombinant Type V) 10009563

gVPLA$_2$
M_r: 14 kDa **Purity:** ≥95%
Supplied in: 50 mM Tris-HCl, pH 8.0, containing 100 mM sodium chloride, 50 mM calcium chloride, and 20% glycerol
Source: Recombinant protein expressed in *E. coli* • Catalyzes the hydrolysis of fatty acids at the *sn*-2 position of glycerophospholipids; responsible for arachidonic acid mobilization leading to PG production in macrophages and mast cells

10 µg
25 µg
50 µg

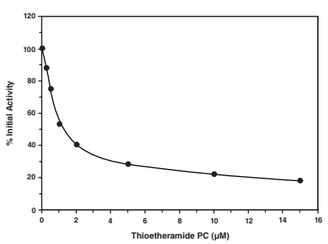
PLA Inhibitors

Product Name	$sPLA_2$ (IC_{50})	$cPLA_2$ (IC_{50})	$iPLA_2$ (IC_{50})
Arachidonyl Trifluoromethyl Ketone Item No. 62160		50 µM (human)	15 µM (mouse)
AX 048 Item No. 13823		$X_i(50) = 0.022$	
Bromoenol lactone Item No. 70700			60 nM (mouse) $K_i = 180$ nM (canine)
CAY10502 Item No. 10008657		4.3 nM (human)	
CAY10590 Item No. 13181			$X_i(50) = 0.003$
CAY10650 Item No. 10743		12 nM	
7,7-dimethyl-5,8-Eicosadienoic Acid Item No. 70500		16 µM (mouse)	
FKGK 11 Item No. 13179			$X_i(50) = 0.0073$
Methyl Arachidonyl Fluorophosphonate Item No. 70660		0.6 µM (human)	0.5 µM (mouse)
Oleyloxyethyl Phosphorylcholine Item No. 70560	6.2 µM (porcine pancreatic)		
Palmityl Trifluoromethyl Ketone Item No. 62650		45 µM (human)	3.8 µM (mouse)
Prostaglandin B_x Item No. 11510	1.4-7 µM (human)		
Pyrrophenone Item No. 13294		4.2 nM	
RSC-3388 Item No. 13343		1.8 nM (human)	
Thioetheramide-PC Item No. 62750	~2 µM (with thio-PC as substrate; cobra venom)		$X_i(50)$ = mole fraction that gives 50% inhibition

$sPLA_2$ (Type V) Inhibitor Screening Assay Kit 10004883

Stability: ≥1 year at -20°C
Summary: Cayman's $sPLA_2$ (Type V) Inhibitor Screening Assay is a convenient colorimetric assay designed for rapid screening of Type V $sPLA_2$ inhibitors in a 96-well format. Each kit contains assay buffer, DTNB, diheptanoyl thio-PC, human $sPLA_2$ (Type V), a 96-well plate, plate cover, and complete instructions.

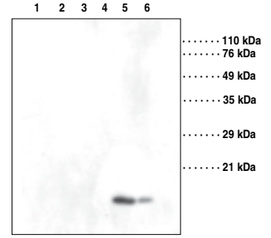
96 wells



$sPLA_2$ (human Type V) Monoclonal Antibody (Clone 3G1.3) 160510

Lyophilized IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human recombinant $sPLA_2$ (Type V) • Host: mouse, clone 3G1.3 • Isotype: IgG_1 • Cross Reactivity: (+) human $sPLA_2$ (Type V); (-) human $sPLA_2$ (Type IIa), $cPLA_2$, and $iPLA_2$ • Application(s): ELISA, IHC, and WB • PLA_2 (type V) is a $sPLA_2$ of approximately 14 kDa. This enzyme, rather than the $sPLA_2$ (type II), is responsible for arachidonic acid mobilization leading to PG production in macrophages and mast cells.

100 µg



Lane 1: $sPLA_2$ (Type II) (1 µg)
Lane 2: A10 smooth muscle lysate ($iPLA_2$) (20 µg)
Lane 3: Bee venom $sPLA_2$ (1 µg)
Lane 4: Semi-pure $cPLA_2$ (5 µg)
Lane 5: $sPLA_2$ (Type V) (40 ng)
Lane 6: $sPLA_2$ (Type V) (8 ng)

Olivia L. May, Ph.D.

Next Generation Arthritis Relief: A Case for mPGES-1 Inhibition and Beyond

Rheumatoid arthritis (RA) is an autoimmune disease characterized by chronic inflammation of synovial tissues associated with loss of cartilage, erosion of juxtaarticular bone, and progressive joint destruction. The synovial membrane becomes a hypertrophic inflammatory tissue infiltrated by macrophages, neutrophils, T lymphocytes, and B lymphocytes, which produce various pro- and anti-inflammatory mediators, matrix-degrading enzymes, and free oxygen species. Eventually, the inflamed tissue overgrows articular cartilage and erodes juxtaarticular bone. Whereas RA is associated with inflamed synovial tissues, osteoarthritis (OA), the "wear and tear" joint disorder, is characterized by inflammation of articular cartilage leading to gradual cartilage erosion. There are similarities and common pathways in the inflammatory processes of both diseases. Eicosanoids, diverse bioactive lipid mediators with both pro- and anti-inflammatory effects, are implicated in the pathophysiology of RA and OA.

Inhibiting eicosanoid biosynthesis the old way

Eicosanoid biosynthesis starts with the cleavage of arachidonic acid from cell membrane phospholipids by cytosolic phospholipase A_2 ($cPLA_2$) and subsequent metabolism by a sequential enzymatic pathway (Figure 1). A key enzyme in this pathway is cyclooxygenase (COX), whose inducible isozyme COX-2 is upregulated in inflammatory joint diseases and is traditionally regarded as one of the earliest biomarkers of the inflammatory cascade in arthritis.[1] COX peroxidase activity catalyzes the generation of the unstable intermediate, prostaglandin (PG) H_2. A specific prostaglandin synthase, PGES, converts PGH_2 to PGE_2, the most abundant pro-inflammatory PG associated with inflammatory conditions. High concentrations of PGE_2 are detected in the synovial fluid of patients with rheumatoid arthritis, where cytokine-activated synovial cells are the main source of PGE_2 in arthritic joints. Inhibition of PGE_2 production and signaling is associated with reduction of pain and inflammation associated with a number of diseases.

Conventional nonsteroidal anti-inflammatory drugs (NSAIDs) and COX-2-specific inhibitors are widely used to treat the pain, swelling, and stiffness associated with arthritis. However because COX catalyzes the production of all terminal PGs, including PGI_2, PGD_2, $PGF_{2\alpha}$, and TXA_2 (Figure 1), global inhibition of COX would interfere with the synthesis of prostanoid mediators of additional, and not necessarily unfavorable, physiological functions. For example, 15-deoxy-$\Delta^{12,14}$-PGJ_2, a metabolite of PGD_2, activates PPARγ, a member of the nuclear hormone receptor superfamily of ligand-activated transcription factors that inhibits the expression of pro-inflammatory cytokines IL-1β and TNF-α in synovial fibroblasts as well as inhibits cytokine-induced expression of inducible nitric oxide synthase (iNOS) and matrix metalloproteinases (MMPs).[2] Furthermore, NSAIDs are unfortunately associated with adverse gastrointestinal and renal side effects and, perhaps most alarmingly, COX-2-specific inhibitors lead to increased incidence of cardiovascular events. For example, COX-2 inhibition results in loss of anti-thrombotic prostacyclin (PGI_2), which plays a key role in the regulation of thrombogenesis.[3] COX-2 selective inhibitors can also be detrimental in the maintenance of ulcer healing and granulation tissue formation.

Downstream targeting for a new generation

Microsomal PGE synthase-1 (mPGES-1), an inducible enzyme for the production of pro-inflammatory PGE_2 from PGH_2, is also upregulated in RA and OA.[4,5] mPGES-1 is a critically important mediator of inflammation, pain, angiogenesis, fever, bone metabolism, tumorigenesis, atherosclerosis, and reproduction. It presents an attractive target to achieve more specific inhibition of PGE_2 production while preserving production of other PGs and, as such, has attracted considerable attention as a "next-generation" anti-inflammatory drug. mPGES-1 null mice are resistant to chronic inflammation of joints in models of collagen-induced arthritis.[6] mPGES-1 deficiency increases in expression of PPARγ, which is known to initiate mechanisms that inhibit inflammatory responses and assist in the resolution of inflammation.[7] Specific activation of PPARγ suppresses IL-1β-induced upregulation of pro-inflammatory COX-2 and mPGES-1 expression and consequent PGE_2 production.[7] Cayman offers a handful of mPGES-1 inhibitors (some of which dually inhibit 5-lipoxygenase, which initiates the synthesis of pro-inflammatory leukotrienes) including: CAY10526 (Item No. 10010088), YS121 (Item No. 13665), and CAY10589 (Item No. 13164). Highly specific mPGES-1 inhibitors continue to be developed as more insight into the enzymatic reaction mechanism/substrate-binding site(s) of mPGES-1 are determined. Recent advances have been made though identifying key catalytic residues,[8,9] resolving the crystal structure,[10] and determining active site conformation[11] which will enable rational inhibitor design in the very near future.

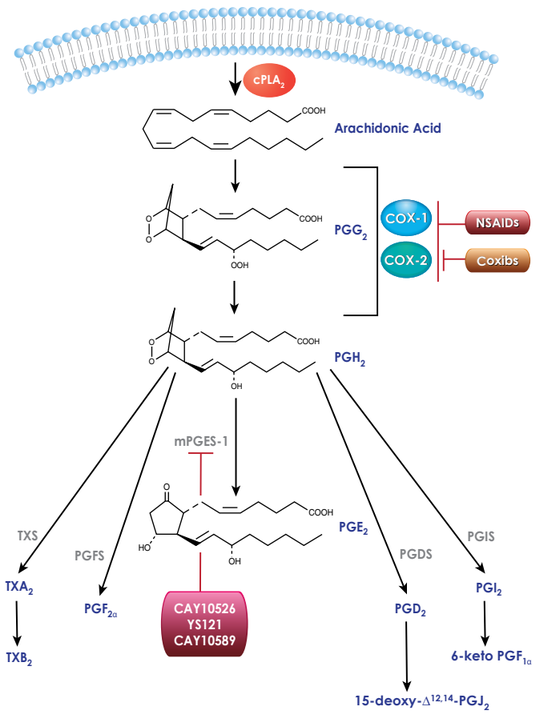


Figure 1. The PGE_2 biosynthetic pathway. During inflammation PGE_2 is produced from arachidonic acid through the subsequent actions of the inducible enzymes COX-2 and mPGES-1. Inhibition of COX-2 leads to a complete shutdown of prostanoid production, whereas specific inhibition of mPGES-1 shunts PGH_2 metabolism towards alternate prostanoids.

What, however, are the collateral consequences of blocking mPEGS-1? In the absence of m-PGES-1, there is a resultant increase the availability of PGH_2 to act as a substrate for the generation of other prostanoids. In mouse embryo fibroblasts, mPGES-1 gene deletion allows for a diversion of prostanoid production from PGE_2 to PGI_2, which plays a key role in thrombogenesis,[5] while in mouse peritoneal macrophages, mPGES-1 deletion increases TXB_2, $PGF_{2\alpha}$, and 6-keto $PGF_{1\alpha}$ levels, prostanoids

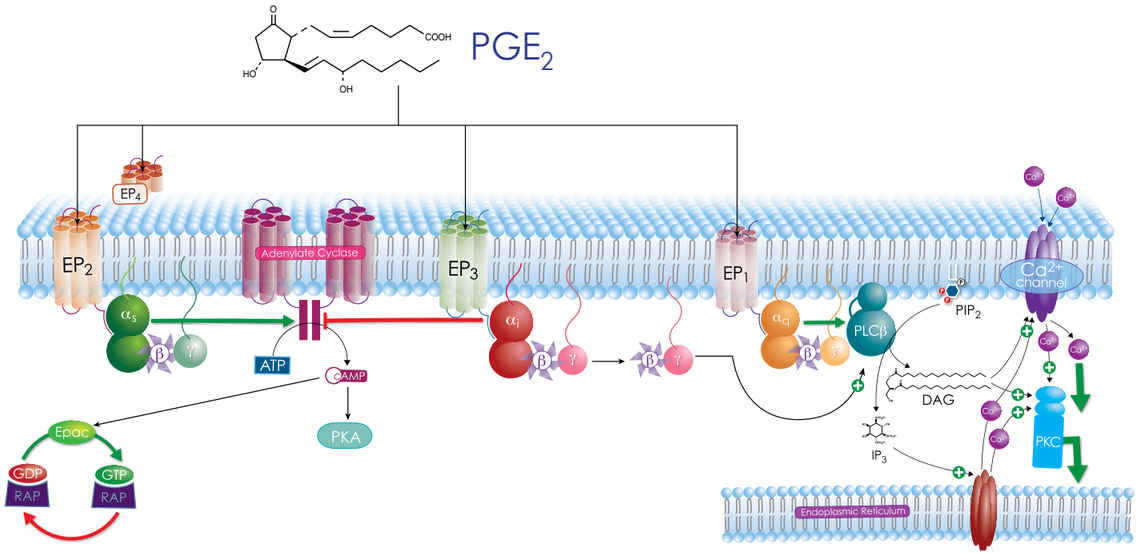


Figure 2. G-protein coupled EP receptor signaling pathway. PGE_2 mediates its biological functions by binding to four different types of membrane-bound, G-protein-coupled receptors. The EP_2 and EP_4 receptors increase cAMP by activating adenylate cyclase *via* $G\alpha_s$ proteins. EP_3 signaling through $G\alpha_i$ (or $G\alpha_s$) has inhibitory (or stimulatory) effects on cAMP levels, whereas EP_1 raises intracellular calcium through $G\alpha_q$.

involved in platelet aggregation, smooth muscle contraction, and thrombogenesis.[12] An absence of mPGES-1-catalyzed PGE_2 production additionally has been shown to upregulate iNOS.[5] However, increased levels of PGI_2 and NO could have undesirable pro-inflammatory effects as well.[13-15]

Modulating E prostanoid (EP) receptor signaling may also be a promising therapeutic strategy to alleviate inflammatory symptoms in arthritis. PGE_2 exerts the majority of its actions through a family of G protein-coupled EP receptors ($EP_{1\text{-}4}$) (Figure 2). The effects of PGE_2 *via* these receptors are mediated through various downstream signaling pathways, including cAMP dependent protein kinase, MAP kinase, PI_3 kinase, and Akt. EP_1 raises intracellular calcium levels by activating $G\alpha_q$, whereas EP_3 reduces or increases cAMP by activating inhibitory ($G\alpha_i$) or stimulatory ($G\alpha_s$) G-proteins depending on the particular splice variant expressed by the cell. The $G\alpha_s$-coupled EP_2 and EP_4 receptors increase cAMP *via* activation of adenylate cyclase and its downstream target, cAMP-dependent protein kinase A (PKA) as well as through Epac (exachange protein directly activated by cAMP). In response to increases in cAMP, Epac activates the small GTPase Rap1, which has a role in the regulation of cytoskeletal structure and cell-cell adhesion. PGE_2 signaling has been shown to activate Rap1 in rheumatoid synovial fibroblasts.[16] Therefore, PGE_2 could be mediating some of its pro-inflammatory effects by altering cytoskeletal structure and function of synovial tissue *via* Rap1. PGE_2 has been reported to auto-regulate the expression of mPGES-1 *via* activation of EP_2 and EP_4 receptors in IL-1β-stimulated rheumatoid synovial fibroblasts. EP_1 and EP_3 receptors have also been indentified in synovial fibroblasts, however their roles seem variable and less prominent compared to EP_2. PGE_2 signaling mediated through EP_2 has recently been shown to have opposite effects on IL-6 and MMP-1 synthesis. EP_2 signaling in TNFα-stimulated rheumatoid synovial fibroblasts has been shown to stimulate mRNA expression of the pro-inflammatory mediator IL-6 while reducing expression of the matrix-degrading enzyme MMP-1.[17] Thus while blocking EP_2 activity may be beneficial in reducing inflammatory stimuli, it may on the other hand exacerbate tissue destruction by promoting MMP activity. This is helpful to understanding the inability of COX inhibitors (and various novel strategies meant to interfere with the PGE_2 pathway) to allay joint destruction.

Several anti-inflammatory, immune modulatory effects of PGE_2 mediated through EP_2 or EP_4 receptors have also been noted. For instance, PGE_2 signaling regulates the production of pro-inflammatory cytokines, enhances the synthesis of anti-inflammatory cytokines (*i.e.*, IL-10), and facilitates both Th1 cell differentiation and Th 17 cell expansion.[18,19] Much remains to be clarified for the involvement of PGE_2-mediated signaling as a mediator of both inflammatory and immune responses. Cayman offers several EP receptor antagonists and agonists (see the Prostaglandin Receptors table on page 50) to aid in this endeavor.

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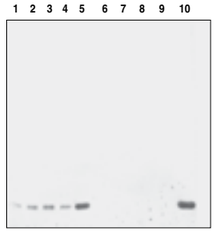
$sPLA_2$ (murine Type V) Polyclonal Antibody 160512

Peptide affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: mouse group V $sPLA_2$ amino acids 79-94 • Host: rabbit • Cross Reactivity: (+) human, mouse, and rat $sPLA_2$ (Type V); (-) bee venom and human synovial (Type II) $sPLA_2$, $iPLA_2$ (A10 cell lysate), and $cPLA_2$ (HeLa cell lysate); $sPLA_2$ (Type X) not tested, but is expected to be negative • Application(s): WB • PLA_2 (type V) is a $sPLA_2$ of approximately 14 kDa. This enzyme, rather than the $sPLA_2$ (type II), is responsible for arachidonic acid mobilization leading to PG production in macrophages and mast cells.

500 µl



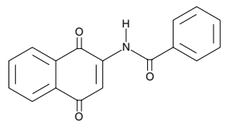
Lane 1: Recombinant human $sPLA_2$ (Type V) (0.025 µg)
Lane 2: Recombinant human $sPLA_2$ (Type V) (0.05 µg)
Lane 3: Recombinant human $sPLA_2$ (Type V) (0.075 µg)
Lane 4: Recombinant human $sPLA_2$ (Type V) (0.1 µg)
Lane 5: Recombinant human $sPLA_2$ (Type V) (0.25 µg)
Lane 6: A10 smooth muscle cell lysate ($iPLA_2$) (50 µg)
Lane 7: Bee venom PLA_2 (1 µg)
Lane 8: Human $sPLA_2$ (Type II) (1 µg)
Lane 9: HeLa cell lysate ($cPLA_2$) (50 µg)
Lane 10: Recombinant human $sPLA_2$ (Type V) (0.25 µg)

• Also Available: **$sPLA_2$ (murine Type V) Blocking Peptide** (360512)

PPM-18 13327

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

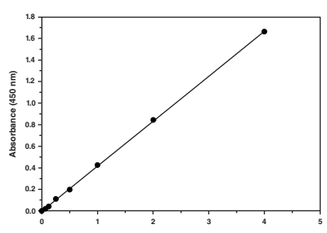
1mg
5 mg
10 mg
25 mg



Progranulin (human) EIA Kit 500940

PGRN
Stability: ≥6 months at 4°C
Summary: PGRN is an autocrine growth factor that plays a role in embryonic development, tissue repair, tumorigenesis, and inflammation. Recently, PGRN has been shown to bind directly to tumor necrosis factor receptor (TNFR) where it antagonizes TNF-α signaling, effectively blocking the pathogenesis of inflammatory arthritis in mice. Furthermore, elevated serum concentrations of PGRN are associated with visceral obesity, elevated plasma glucose, and dyslipidemia. In the central nervous system, PGRN is thought to be involved in neurotrophic activity and neuroinflammation. Cayman's PGRN (human) EIA Kit is an immunometric assay which can be used to measure progranulin in human serum, plasma, or cell culture supernatants. The assay exhibits a detection limit of 32 pg/ml and an assay range of 0-4 ng/ml.

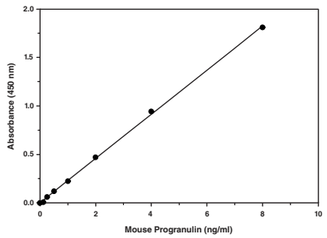
96 wells



Progranulin (mouse) EIA Kit 500950

PGRN
Stability: ≥6 months at 4°C
Summary: PGRN is an autocrine growth factor that plays a role in embryonic development, tissue repair, tumorigenesis, and inflammation. Recently, PGRN has been shown to bind directly to TNFR where it antagonizes TNF-α signaling, effectively blocking the pathogenesis of inflammatory arthritis in mice. Furthermore, elevated serum concentrations of PGRN are associated with visceral obesity, elevated plasma glucose, and dyslipidemia. In the central nervous system, PGRN is thought to be involved in neurotrophic activity and neuroinflammation. Cayman's PGRN (mouse) EIA Kit is an immunometric assay which can be used to measure progranulin in mouse serum or cell culture supernatants. The assay exhibits a detection limit of 60 pg/ml and an assay range of 0-8 ng/ml.

96 wells



PGD_2 - Related Inhibitors and Receptor Antagonists

Item No.	Product Name	Notes
13160	AT-56	Bioavailable L-PGDS inhibitor (K_i = 75 µM)
10156	BAY-u3405	CRTH2/DP_2 receptor antagonist (IC_{50} = 100-170 nM); AKA Ramatroban
12060	BW A868C	First selective DP_1 receptor antagonist
10006735	CAY10471	CRTH2/DP_2 receptor antagonist (K_i = 0.6 nM); analog of BAY-u3405
10012553	CAY10595	CRTH2/DP_2 receptor antagonist (K_i = 10 nM)
10012539	CAY10597	CRTH2/DP_2 receptor antagonist (K_i = 37 nM)
10134	HQL-70	Selective inhibitor of H-PGDS (IC_{50} = 51 µM)
10009835	MK 0524	Selective DP_1 receptor antagonist (K_i = 0.57 nM)
13044	Tranilast	PGD synthase inhibitor (IC_{50} = 0.1 mM)

PGD_2 Receptor Agonists

Item No.	Product Name	Notes
12010	Prostaglandin D_2	A Natural Ligand
12050	BW 245C	Selective DP_1 receptor agonist (K_i = 0.9 nM)
12055	BW 246C	70-fold less active C-8 diastereomer of BW 245C
10118	15(R)-Prostaglandin D_2	Potent agonist at the CRTH2/DP_2 receptor
12610	13,14-dihydro-15-keto Prostaglandin D_2	Selective agonist for the CRTH2/DP_2 receptor; AKA DK-PGD_2
12720	15(R)-15-methyl Prostaglandin D_2	Potent, selective agonist for the CRTH2/DP_2 receptor; EC_{50} values are 3-5 fold lower than PGD_2
12750	16,16-dimethyl Prostaglandin D_2	Enhances platelet aggregation and increases systemic blood pressure in rats

Also Available: 15(S)-15-methyl Prostaglandin D_2 (13730)

Prostaglandin D Synthase (hematopoietic-type; human recombinant) 10006593

Hematopoietic-PGDS, H-PGDS
M_r: 24.3 kDa **Purity:** ≥95%
Supplied in: 50 mM sodium phosphate, pH 7.2, containing 20% glycerol, 100 mM sodium chloride, 1 mM DTT and 0.5 mM EDTA
Source: Human recombinant N-terminal His-tagged protein expressed in *E. coli*

50 µg
100 µg
250 µg

Prostaglandin D Synthase (hematopoietic-type; mouse recombinant) 10004347

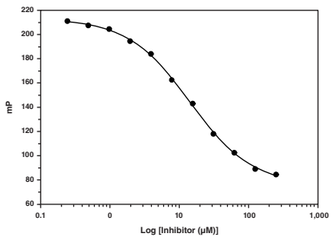
Hematopoietic-PGDS, H-PGDS
M_r: 23.5 kDa **Purity:** ≥85%
Supplied in: 50 mM sodium phosphate, pH 7.2, containing 100 mM sodium chloride, 0.5 mM EDTA, and 50% glycerol
Source: Recombinant enzyme expressed in *E. coli*

50 µg
100 µg
250 µg

Prostaglandin D Synthase (hematopoietic-type) FP-Based Inhibitor Screening Assay Kit - Green 600007

H-PGDS
Stability: ≥6 months at -20°C
Summary: PGD_2 is synthesized by H-PGDS in mast cells and is released in large quantities during allergic and asthmatic anaphylaxis. Cayman's H-PGDS FP-Based Inhibitor Screening Assay provides a rapid method for screening H-PGDS inhibitors. In this assay, an H-PGDS inhibitor-fluorescein conjugate serves as a specific fluorescent probe for the enzyme. Displacement of the probe by any unlabeled H-PGDS inhibitor leads to a decrease in the FP state of the probe, providing a direct signal for binding of the inhibitor to the active site of the enzyme.

384 wells
1,920 wells



Prostaglandin D Synthase (lipocalin-type; human recombinant) 10006788

Lipocalin-PGDS, L-PGDS
M_r: 46 kDa **Purity:** ≥95%
Supplied in: 50 mM sodium phosphate, pH 7.2, containing 20% glycerol, 150 mM sodium chloride, 1 mM DTT, and 0.5 mM EDTA
Source: Recombinant enzyme expressed in *E. coli*

100 µg
250 µg
500 µg

Prostaglandin D Synthase (lipocalin-type; mouse recombinant) 10006787

Lipocalin-PGDS, L-PGDS
M_r: 46 kDa **Purity:** ≥95%
Supplied in: 50 mM sodium phosphate, pH 7.2, containing 20% glycerol, 150 mM sodium chloride, 1 mM DTT, and 0.5 mM EDTA
Source: Recombinant GST-tagged enzyme expressed in *E. coli*

100 µg
250 µg
500 µg

Prostaglandin D Synthase (lipocalin-type; rat recombinant) 10010548

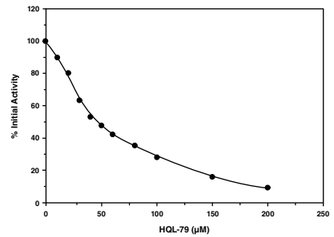
Lipocalin-PGDS, L-PGDS
M_r: 47.5 kDa **Purity:** ≥95%
Supplied in: 50 mM sodium phosphate, pH 7.2, containing 100 mM sodium chloride, 1 mM DTT, 0.5 mM EDTA, and 20% glycerol
Source: Recombinant N-terminal GST-tagged protein expressed in *E. coli*

100 µg
250 µg
500 µg

Prostaglandin D Synthase Inhibitor Screening Assay Kit 10006595

Stability: ≥6 months at -80°C
Summary: Cayman's PGDS Inhibitor Screening Assay is a complete package for the evaluation of PGDS isozyme-specific inhibitors. Each kit includes highly purified H-PGDS and L-PGDS, as well as PGH_2 which serves as the enzyme substrate. A complete EIA for the direct quantification of PGD_2 without prior methoxymation is included in the kit.

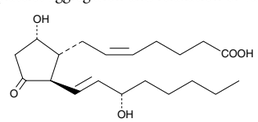
96 wells



Prostaglandin D_2 12010

[41598-07-6]
MF: $C_{20}H_{32}O_5$ **FW:** 352.5 **Purity:** ≥99%*
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: The major eicosanoid product of mast cells that is released in large quantities during allergic and asthmatic anaphylaxis; causes vasodilation, flushing, hypotension, and syncopal episodes; also produced in the brain where it produces normal physiological sleep and lowering of body temperature; additional actions include inhibition of platelet aggregation and relaxation of vascular smooth muscle

1 mg
5 mg
10 mg
50 mg



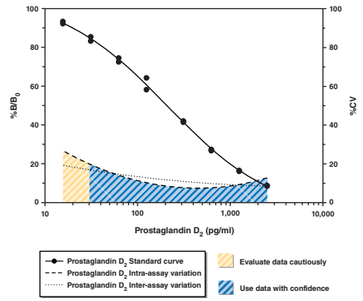
• Also Available: **Prostaglandin D_2-d_4** (312010)
Prostaglandin D_2-d_4 Lipid Maps MS Standard (10007272)
Prostaglandin D_2 Lipid Maps MS Standard (10007202)

**All 5-cis 2-series PGs (those containing a 5,6-double bond) will contain a small amount of the 5-trans isomer. This isomer is generally undetectable using normal phase silica columns and plates, but may be resolved using RP-HPLC. The purity for all such 2-series PGs excludes the 1-3% trans isomer which will generally be present.*

Prostaglandin D_2 EIA Kit 512031

Stability: ≥6 months at -80°C
Sensitivity: 50% B/B_0: 240 pg/ml • 80% B/B_0: 55 pg/ml
Summary: PGD_2 is biosynthesized in the brain by a soluble, 26 kDa glutathione-independent lipocalin-type PGD_2 synthase. This PGD_2 accumulates in the cerebrospinal fluid (CSF), where it induces physiologic sleep in rats and humans. PGD_2 is also synthesized in mast cells and leukocytes by a cellular, myeloid-type, glutathione-dependent PGD synthase. This PGD_2 which is formed in the intracellular and vascular compartments is rapidly metabolized to 11β-$PGF_{2\alpha}$ and other metabolites. Measurement of the parent eicosanoid PGD_2 is appropriate in cell culture lysates and in CSF, where concentrations of several hundred pg/ml have been measured. Cayman's PGD_2 EIA Kit is a competitive assay that can be used for quantification of PGD_2 in cell culture lysates and enzymatic reactions.

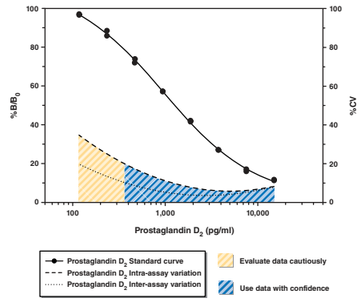
96 solid/strip wells
480 solid/strip wells



Prostaglandin D_2 Express EIA Kit 512041

Stability: ≥6 months at -80°C
Sensitivity: 50% B/B_0: 1,300 pg/ml • 80% B/B_0: 350 pg/ml
Summary: Cayman's PGD_2 Express EIA Kit is a competitive assay that can be used for quantification of PGD_2 in cell culture lysates and enzymatic reactions. This EIA offers the convenience of a fast assay with a two hour incubation time and one hour development time, while still achieving an IC_{50} value (50% B/B_0) of approximately 1,300 pg/ml and a detection limit (80% B/B_0) of approximately 350 pg/ml.

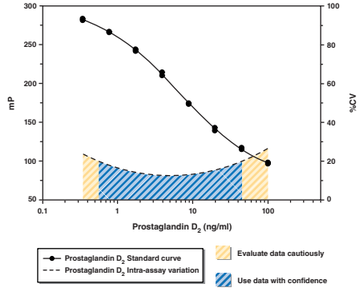
96 solid/strip wells
480 solid/strip wells



Prostaglandin D_2 FPIA Kit - Red 512051

PGD_2 Fluorescence Polarization Immunoassay - Red
Stability: ≥1 year at -80°C **Limit of Detection:** 550 pg/ml **Z' Factor:** 0.62
Summary: Cayman's PGD_2 FPIA is especially designed for high-throughput screening assays for PGD_2 from cell culture and purified enzyme preparation. The PGD_2-FPIA is robust (Z' = 0.62), exhibits greater than 180 mP over a range of 340 pg/ml to 100 ng/ml PGD_2, and has a detection limit of 550 pg/ml.

96 wells
480 wells



•Also Available: **Prostaglandin D_2 FIPA Kit - Green** (500581)

Prostaglandin D_2-MOX EIA Kit 512011

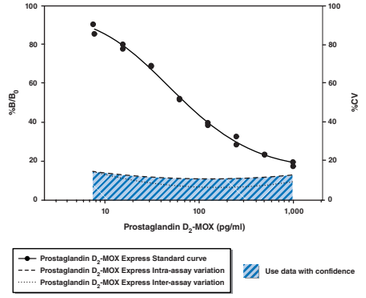
Stability: ≥1 year at -20°C
Sensitivity: 50% B/B_0: 15 pg/ml • 80% B/B_0: 3.1 pg/ml
Summary: This PGD_2-MOX EIA is a highly sensitive assay that is based on the conversion of PGD_2 to a stable MOX derivative. Treatment of the sample with MOX HCl converts PGD_2 into PGD_2-MOX, preventing its further chemical degradation. The assay is suited for measurement of PGD_2 from complex sample types, such as plasma and urine.

96 solid/strip wells
480 solid/strip wells

Prostaglandin D_2-MOX Express EIA Kit 500151

Stability: ≥1 year at -20°C
Sensitivity: 50% B/B_0: 75 pg/ml • 80% B/B_0: 16 pg/ml
Summary: Cayman's PGD_2-MOX Express EIA is a competitive assay that permits the rapid measurement of PGD_2 from biological samples, requiring only one hour incubation and development times for each step.

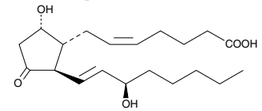
96 solid/strip wells
480 solid/strip wells



15(R)-Prostaglandin D_2 10118

MF: $C_{20}H_{32}O_5$ **FW:** 352.5 **Purity:** ≥98%*
A solution in methyl acetate **Stability:** ≥1 year at -20°C
Summary: A potent and selective CRTH2/DP_2 receptor agonist, that is five equipotent with PGD_2 at this receptor

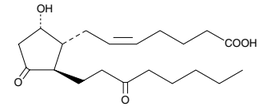
1 mg
5 mg
10 mg
50 mg



13,14-dihydro-15-keto Prostaglandin D_2 12610

[59894-07-4]
MF: $C_{20}H_{32}O_5$ **FW:** 352.5 **Purity:** ≥98%*
A solution in methyl acetate **Stability:** ≥1 year at -80°C
Summary: A metabolite of PGD_2 which is formed through the 15-hydroxy PGDH pathway; a selective agonist for the CRTH2/DP_2 receptor

1 mg
5 mg
10 mg
50 mg

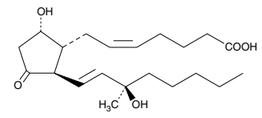


•Also Available: **13,14-dihydro-15-keto Prostaglandin D_2-d_4** (10007978)
13,14-dihydro-15-keto Prostaglandin D_2 Lipid Maps MS Standard (10007202)

15(R)-15-methyl Prostaglandin D_2 12720

[210978-26-0]
MF: $C_{21}H_{34}O_5$ **FW:** 366.5 **Purity:** ≥95%*
A solution in methyl acetate **Stability:** ≥1 year at -20°C
Summary: A potent, selective agonist for the CRTH2/DP_2 receptor (EC_{50} for eosinophil chemotaxis is 1.7 nM)

500 µg
1 mg
5 mg
10 mg

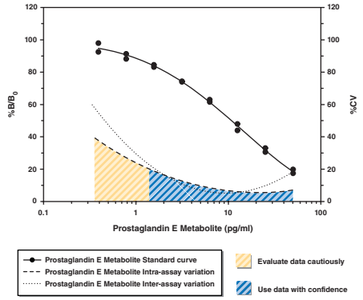


•Also Available: **15(S)-15-methyl Prostaglandin D_2** (12730)

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 solid/strip wells
480 solid/strip wells



Prostaglandin E Synthase (cytosolic; human recombinant, inactive protein) 10010498

cPGES; cPGE Synthase; Telomerase-binding protein p23, p23, Hsp90 Co-chaperone
M_r: 22.3 kDa **Purity:** ≥75%
Supplied in: $NaPO_4$, pH 7.2, containing 100 mM sodium chloride and 20% glycerol
Source: Recombinant His-tagged protein expressed in *E. coli* • A glutathione-dependent enzyme thought to modulate Hsp90 activity during the last stages of the chaperoning pathway; also shown to have PGES activity, catalyzing the isomerization of PGH_2 to PGE_2; expressed in a variety of tissues and cells and its levels are unaffected by treatment with IL-1β and TNF-α

100 µg
250 µg
500 µg

Prostaglandin E Synthase-1 (microsomal) (human recombinant) 10007939

MGSTL-1, PIG12, Prostaglandin H/E Isomerase; Membrane-Associated PGES-1
M_r: ~21 kDa **Purity:** 16,000 x g supernatant
Supplied in: 50 mM sodium phosphate, pH 7.2, containing 100 mM sodium chloride and 20% glycerol
Summary: Recombinant enzyme expressed in *Sf*21 cells • A perinuclear protein belonging to the membrane-associated proteins involved in the conversion of COX-derived PGH_2 to PGE_2; requires glutathione as an essential cofactor for activity and is up-regulated in response to various proinflammatory stimuli with a concomitant increased expression of COX-2; down-regulated by glucocorticoids

250 U
500 U
1 kU

**All 5-cis 2-series PGs (those containing a 5,6-double bond) will contain a small amount of the 5-trans isomer. This isomer is generally undetectable using normal phase silica columns and plates, but may be resolved using RP-HPLC. The purity for all such 2-series PGs excludes the 1-3% trans isomer which will generally be present.*

Prostaglandin D and E Synthase Antibodies

Item No.	Item name	Antigen/Host	Cross-reactivity	Applications
160013	PGDS (hematopoietic-type) Polyclonal Antibody	human hematopoietic-type PGDS amino acids 30-41 • Host: rabbit	(+) human, mouse, rat, and baboon H-PGDS; other species not tested	WB; other applications not tested
10004345	PGDS (hematopoietic-type; human) Monoclonal Antibody	recombinant human H-PGDS • Host: mouse	(+) human and mouse H-PGDS; other species not tested	WB and IHC
10004337	PGDS (hematopoietic-type; human) Polyclonal Antibody	recombinant human H-PGDS • Host: rabbit	(+) human and mouse H-PGDS; other species not tested	WB and IHC
10004349	PGDS (hematopoietic-type; mouse) Monoclonal Antibody	recombinant mouse H-PGDS • Host: rat	(+) human and mouse H-PGDS; other species not tested	WB and IHC
10004348	PGDS (hematopoietic-type; mouse) Polyclonal Antibody	recombinant mouse H-PGDS • Host: rabbit	(+) human and mouse H-PGDS; other species not tested	WB and IHC
160003	PGDS (lipocalin-type) Polyclonal Antibody	human lipocalin-type PGD synthase amino acids 30-41 • Host: rabbit	(+) human and mouse L-PGDS; (-) H-PGDS; other species not tested	WB; other applications not tested
10004342	PGDS (lipocalin-type; human) Monoclonal Antibody	recombinant human L-PGDS • Host: rat	(+) human and mouse L-PGDS; other species not tested	WB and IHC
10004344	PGDS (lipocalin-type; mouse) Polyclonal Antibody	recombinant mouse L-PGDS • Host: rabbit	(+) human and mouse L-PGDS; other species not tested	WB and IHC
18219	Prostaglandin E Synthase (cytosolic) Monoclonal Antibody (Clone JJ6)	human full length p23 protein • Host: mouse	(+) human, mouse, rabbit, chicken, guinea pig, and *S. cerevisiae* (lower) cPGES	ELISA, IP, and WB
160150	Prostaglandin E Synthase (cytosolic) Polyclonal Antibody	human cPGES amino acids 58-67 • Host: rabbit	(+) human, mouse, and ovine cPGES; (-) recombinant human mPGES	WB and IHC
10209	Prostaglandin E Synthase (cytosolic, FL) Polyclonal Antibody	recombinant human cPGES • Host: rabbit	(+) human and mouse cPGES; (-) mPGES-1 and -2	WB and ICC
10004350	Prostaglandin E Synthase-1 (microsomal) Monoclonal Antibody	recombinant human mPGES-1 • Host: mouse	(+) human mPGES-1; (-) ovine mPGES-1; other species not tested	WB, ICC, and IHC
160140	Prostaglandin E Synthase-1 (microsomal) Polyclonal Antibody	human mPGES amino acids 59-75 • Host: rabbit	(+) human, mouse, rat, and ovine mPGES; (-) cPGES; other species not tested	WB and IHC; other applications not tested
160145	Prostaglandin E Synthase-2 (microsomal) Polyclonal Antibody	human mPGES-2 amino acids 221-235 • Host: rabbit	(+) human, mouse, rat, ovine, bovine, and Cos-7 (African green monkey) mPGES-2; suspected positive with macaque but not yet tested (-) mPGES-1, cytosolic PGES	WB; other applications not tested

Also Avaiable:
Prostaglandin D Synthase (hematopoietic-type; human recombinant) Western Ready Control (10009625)
Prostaglandin D Synthase (lipocalin-type; human) Western Ready Control (10009741)
Prostaglandin E Synthase (cytosolic) Western Ready Control (10009735)
Prostaglandin E Synthase-1 (microsomal) Western Ready Control (10009734)

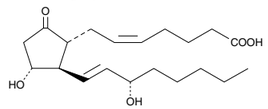
Prostaglandin D and E Synthase Enzymes

Item No.	Item Name	Source	M_r	Purity
10004347	Prostaglandin D Synthase (hematopoietic-type; mouse recombinant) CAYMAN EXCLUSIVE	recombinant enzyme expressed in *E. coli*	23.5 kDa	>85%
10006593	Prostaglandin D Synthase (hematopoietic-type; human recombinant)	recombinant enzyme expressed in *E. coli*	23.3 kDa	>95%
10006787	Prostaglandin D Synthase (lipocalin-type; mouse recombinant)	recombinant GST-tagged enzyme expressed in *E. coli*	46 kDa	>95%
10006788	Prostaglandin D Synthase (lipocalin-type; human recombinant)	recombinant enzyme expressed in *E. coli*	46 kDa	>95%
10010548	Prostaglandin D Synthase (lipocalin-type; rat recombinant) CAYMAN EXCLUSIVE	recombinant N-terminal GST-tagged enzyme expressed in *E. coli*	47.5 kDa	>95%
10007939	Prostaglandin E Synthase-1 (microsomal) (human recombinant)	recombinant enzyme isolated from a baculovirus overexpression system in Sf21 cells	~21 kDa	16,000 x g supernatant
10010498	Prostaglandin E Synthase (cytosolic) in *E. coli* (human recombinant, inactive protein)	recombinant N-terminal His-tagged enzyme expressed in *E. coli*	22.3 kDa (His-tagged); 18 kDa (native)	

Prostaglandin E_2 14010

[363-24-6] Dinoprostone
MF: $C_{20}H_{32}O_5$ **FW:** 352.5 **Purity:** ≥99%*
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: One of the primary COX products of arachidonic acid and one of the most widely investigated PGs; activity influences inflammation, fertility and parturition, gastric mucosal integrity, and immune modulation

1 mg
5 mg
10 mg
50 mg

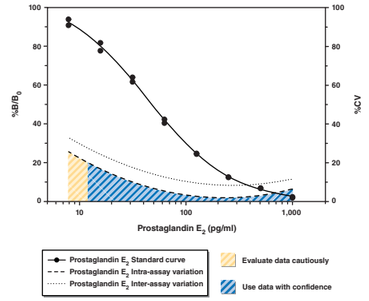


•Also Available: **Prostaglandin E_2-d_4** (314010)
Prostaglandin E_2 Lipid Maps MS Standard (10007211)

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, culture media, and other samples.

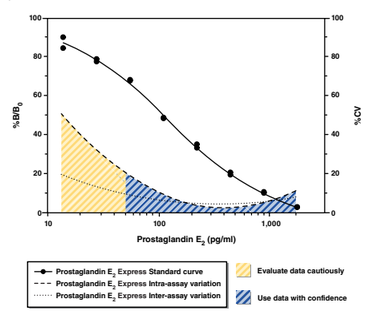
96 solid/strip wells
480 solid/strip wells



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 is a competitive assay that permits the rapid measurement of PGE_2 from biological samples, requiring only 1 hour incubation and development times for each step.

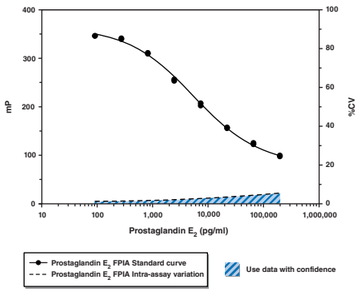
96 solid/strip wells
480 solid/strip wells



Prostaglandin E_2 FPIA Kit - Red 10004517

PGE_2 Fluorescence Polarization Immunoassay - Red
Stability: ≥6 months at -20°C **Limit of Detection:** 100 pg/ml **Z' Factor:** 0.71
Summary: Cayman's PGE_2 FPIA is an excellent method for rapid, high-throughput screening of PGE_2 samples. This assay utilizes the red-shifted dye rhodamine as the label.

384 wells
1,069 wells

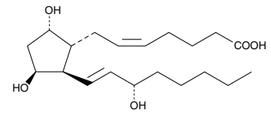


•Also Available: **Prostaglandin E_2 FPIA Kit - Green** (500501)

11β-Prostaglandin $F_{2\alpha}$ 16520

[38432-87-0]
MF: $C_{20}H_{34}O_5$ **FW:** 354.5 **Purity:** ≥99%*
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: Primary plasma metabolite of PGD_2; levels increase nearly 3-fold upon allergan-induced bronchoconstriction in asthmatics

1 mg
5 mg
10 mg
25 mg

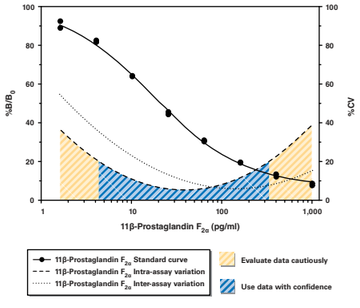


•Also Available: **11β-Prostaglandin $F_{2\alpha}$ Lipid Maps MS Standard** (10007224)

11β-Prostaglandin $F_{2\alpha}$ EIA Kit 516521

Stability: ≥1 year at -20°C
Sensitivity: 50% B/B_0: 32 pg/ml • 80% B/B_0: 5.5 pg/ml
Summary: 11β-$PGF_{2\alpha}$ is the primary plasma metabolite of PGD_2 *in vivo*, the levels of which can increase from 6 pg/ml in a normal healthy volunteer to 490 ng/ml in patients with systemic mastocytosis. This assay allows sensitive detection of 11β-$PGF_{2\alpha}$ in the most common sample matrix, which is urine.

96 solid/strip wells
480 solid/strip wells



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vol. 13 In

Thomas G. Brock, Ph.D.

NF-κB

Few pathways have been studied in as much detail as the NF-κB pathway. First described in 1988, the fundamentals of the canonical (or, classical) pathway were rapidly fleshed out (Figure 1). The central unit is composed of a homo- or heterodimer of NF-κB/Rel transcription factors. In vertebrates, these include p50 (NF-κB1), p52 (NF-κB2), p65 (RelA), RelB, and c-Rel (Rel). All share a conserved 300-amino acid region known as the Rel homology domain, which mediates DNA binding, dimerization, and nuclear import of NF-κB. The major cellular form of NF-κB is a heterodimer consisting of the DNA binding subunit p50 and the transactivator p65. Usually, the NF-κB dimer is retained in the cytoplasm through association with its inhibitor IκB. Upon stimulation by various NF-κB activating signals (*e.g.*, after cellular activation by TNF-α, IL-1, or LPS), IκB is phosphorylated and degraded through a ubiquitin/proteasomal process. Release of IκB reveals the nuclear localization signals on NF-κB, allowing import into the nucleus and activation of transcription of target genes.

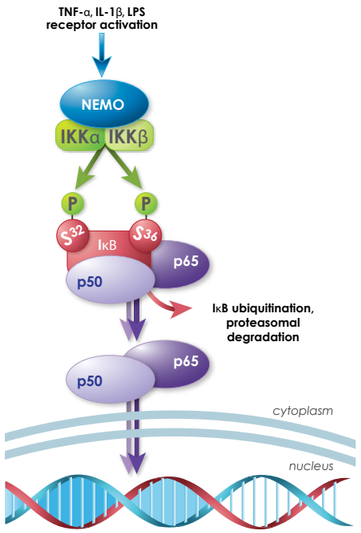

Figure 1. The canonical pathway for NF-κB activation

The phosphorylation of IκB is mediated by the IκB kinase (IKK) complex. The core of this critical complex consists of NF-κB essential modulator (NEMO, or IKKγ), IKKα, and IKKβ. In fact, this high molecular weight IKK complex contains multiple IKKα-IKKβ heterodimers and NEMO homodimers. Several additional proteins, acting as regulatory or adapter proteins, interact with the IKK complex and, most commonly, with NEMO in particular. NEMO is needed for the activation of the IKK complex, and subsequently of NF-κB, by a wide range of stimuli, while IKKβ is the predominant kinase in the canonical pathway.

Some Details on Key Players: NF-κB Inhibitor Kinases

IKKα (IKKA, IKK1, IKBKA, CHUK): conserved helix-loop-helix ubiquitous kinase). Serine/threonine protein kinase that phosphorylates p65 and p100; activated only when phosphorylated; phosphorylated by MAP3K14/NIK, AKT, and MEKK1, and autophosphorylated; dephosphorylated by PP2A; most commonly, heterodimerizes with IKKβ; may be cytoplasmic or intranuclear; in non-canonical signaling, MAP3K14-activated IKKα homodimers phosphorylate p100 associated with RelB, inducing proteolytic processing of p100 to p52 and the formation of p52-RelB complexes; key phosphorylation sites on IKKα include pThr^{23} (regulates enzyme activation, apoptosis, and transcription) and pSer^{180} (affects enzyme activation, chromatin organization, transcription, and cell motility); acetylation at Thr^{179} by *Yersinia* yopJ prevents phosphorylation and activation; also phosphorylates NCOA3, histone H3, IRF7, cyclin D1, ERα, β-catenin, and NCOR2/SMRT[1]

IKKβ (IKKB, IKK2): Kinase that phosphorylates IκBα as well as p105; heterodimerizes with IKKα; phosphorylated on Ser^{177} and Ser^{181} by MEKK1 and/or MAP3K14/NIK, which enhances activity; once activated, autophosphorylates on C-terminal serine cluster, which decreases activity and prevents prolonged activation of the inflammatory response; acetylated on Thr^{180} by *Yersinia* yopJ, preventing phosphorylation and activation; mono-ubiquitination by TRIM21, blocked by *Yersinia* yopJ, inhibits Tax-induced signaling; phosphorylates many targets, including NCOA3, BCL10, IRS1, DOK1, FOXO3a, and 14-3-3β[1]

NEMO (NF-κB essential modulator, IKKγ, IKKAP): Regulatory subunit of the IKK complex; mutations in the gene encoding NEMO result in immunodeficiencies; forms a disulfide-linked homodimer; may be cytoplasmic or intranuclear; sumoylated NEMO accumulates in the nucleus in response to genotoxic stress; phosphorylation at Ser^{68} attenuates N-terminal homodimerization; polyubiquitination on either Lys^{285} or Lys^{399} facilitates interactions with activating proteins; sumoylation on Lys^{277} and Lys^{309} allows phosphorylation of Ser^{85} by ATM, leading to replacement of sumoylation by mono-ubiquitination on Lys^{277} and Lys^{309} and nuclear export of NEMO;[2,3] several proteins bind and inhibit NEMO[4]

NF-κB Inhibitors

IκBα (IκBA, MAD-3): Principle inhibitor of NF-κB/Rel complexes; phosphorylation on Ser^{32} and Ser^{36} leads to polyubiquitination, starting at Lys^{21} and Lys^{22}, followed by proteasomal degradation; shuttles between cytoplasm and nucleus by a nuclear localization signal and a CRM1-dependent nuclear export signal; phosphorylation on Tyr^{42}, by p56^{Lck} (human) or Src (mouse), in response to hypoxia, H_2O_2, ultraviolet light, and other factors can also cause dissociation from NF-κB subunits with NF-κB activation, without IκBα ubiquitination or degradation;[5,6] gene expression of IκBα is induced by activated NF-κB, resulting in subsequent termination of NF-κB signaling

IκBβ (IκBB, NFKBIB, TRIP9): Interacts with p65 and c-Rel; hypophosphorylated intranuclear IκBβ binds nuclear NF-κB, preventing it from inhibition by newly synthesized IκBα; Ser^{313} and Ser^{315} in a PEST domain are basally phosphorylated by casein kinase II, which is necessary for normal inhibitory activity of IκBβ;[7] mitochondrial stress activates the calcium-dependent phosphatase calcineurin, which dephosphorylates Ser^{313} and Ser^{315} and activates NF-κB;[8] phosphorylation on Ser^{19} and Ser^{23} leads to ubiquitination and degradation; interacts with IκB-interacting Ras-like NKIRAS1 and NKIRAS2, preventing its phosphorylation and degradation

Transcription Factors

p50 (NFκB1): NFκB1 gene encodes a 105 kD protein which can undergo co-translational processing by the 26S proteasome to produce a 50 kD protein, the N-terminal 433 residues; either IKKα or IKKβ can phosphorylate p105 on Ser^{927}, leading to mono-ubiquitination and proteasomal processing; the 105 kD protein can also act as a Rel protein-specific transcription inhibitor; glycogen synthase kinase-3β (GSK3β), active in resting cells, phosphorylates p105 on Ser^{903} and Ser^{907}, stabilizing p105 under resting conditions and priming p105 for degradation, with concomitant p50 generation, upon TNF-α stimulation;[9] p65-p50 and RelB-p50 heterodimers are transcriptional activators, whereas the p50-p50 homodimer is a transcriptional repressor (unless associated with BCL3); phosphorylation of Ser^{337} by PKA is critical for DNA binding by p50, and this is inhibited by tumorigenic adenovirus type 12 E1A

p65 (RelA, NFκB3): Commonly heterodimerizes with p50; p65 homodimers initiate transcription of fibronectin, type VII collagen, ICAM-1, and IL-8; p65 dimerized with p50, p65 or c-Rel acts as a transcriptional activator; may be mono-methylated on Lys^{310} by SETD6, allowing binding by EHMT1 and repressed transcription at target genes; phosphorylation on Ser^{311} disrupts EHMT1 binding, promoting transcription; phosphorylation at Ser^{536} stimulates acetylation on Lys^{310} and interaction with CBP, enhancing transcription; acetylation on Lys^{122} and Lys^{123} by CBP impairs p65 transactivation, with deacetylation mediated by HDAC3; acetylation at Lys^{218} and Lys^{221} inhibits IκBα binding and increases p65 transcription; ultraviolet light, through MSK2 or PKA, increases phosphorylation on Ser^{276} and stabilizes p65, allows binding by CBP, and increases or prolongs transcription;[10] interaction with TFIID is promoted by pSer^{536}, *via* IKK; IKK and GSK3β cause pSer^{468}, a prerequisite for ubiquitination and degradation of p65

Non-canonical (Alternative) Pathway

Receptors for certain stimuli, including lymphotoxin-β, CD40-L, LPS, and B-cell-activating factor of the TNF family (BAFF), as well as latent membrane protein-1 (LMP1) of Epstein-Barr virus, initiate an IκB-independent, or non-canonical, pathway (Figure 2). This pathway focuses on NF-κB2/p100, which associates with RelB in the cytoplasm, effectively preventing nuclear import and activation of gene transcription. Receptor signaling activates MAP3K14, also known as NF-κB-inducing kinase, or NIK, which phosphorylates IKKα in turn. IKKα phosphorylates the C-terminus of p100, inducing ubiquitin-dependent processing of p100 to p52 by the 26S proteasome. p52/RelB heterodimers are then able to tranlocate into the nucleus, bind to distinct promoters, and initiate the transcription of a specific subset of genes.

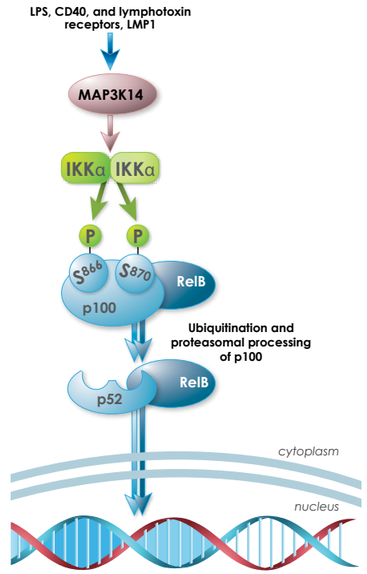

Figure 2. The non-canonical pathway for NF-κB activation

Some Non-Classical or Minor NF-kB Proteins

MAP3K14 (NF-κB-inducing kinase, NIK): Homologous to other MAPKK kinases; interacts with several TNF receptor-associated factors (TRAF), including TRAF2; autophosphorylated, with phosphorylation of Thr^{559} required for kinase activity; Lys^{63} polyubiquitination stabilizes and activates, while Lys^{48} polyubiquitination leads to degradation

TAK-1 (TGF-β-activated kinase-1, MAP3K7, MAPKKK7): Complexed with TAB proteins, phosphorylates IKKβ and/or IKKγ in a ubiquitin-dependent pathway stimulated by TGF-β or genotoxic stress, initiating the activation of the canonical NF-κB pathway[11,12]

IκBζ (IκBZ, INAP, MAIL): Induced by TNF-α, IL-1β, and LPS in leukocytes; inhibits transactivation of p65 and p50;[13] acts as an activator of IL-6 production while decreasing TNF-α production in response to LPS; co-localizes with NCOR2/SMRT and HDAC5 in the nucleus[13]

IKKε (IKKE, IKKi): A non-canonical IKK that is essential for regulating antiviral signaling pathways; autophosphorylated; may be cytoplasmic or in the nucleus, targeting PML nuclear bodies upon DNA damage, by TOPORS-mediated sumoylation; protects cells against DNA damage-induced cell death; identified as a breast cancer oncogene, amplified and overexpressed in over 30% of breast carcinomas and breast cancer cell lines; phosphorylates p65 on Ser^{468} and Ser^{536};[14] phosphorylates IRF3 and IRF7, which form a complex with NF-κB to enhance production of type I interferons; phosphorylates c-Jun, facilitating the clearance of NCoR from promoters

p52 (NFκB2): NFκB2 gene encodes a 100 kD protein; lymphotoxin-β receptor agonists and LPS induce p100 processing to p52 through proteasomal degradation; p52 consists of the N-terminal 454 residues of p100; RelB-p52 activates, while p52-p52 represses, transcription; in the non-canonical pathway, MAP3K14-activated IKKα homodimer phosphorylates p100 associated with RelB, inducing processing to p52 to give p52-RelB; IKKα phosphorylates Ser^{866} and Ser^{870}; GSK3β phosphorylates Ser^{222}, disrupting p52 homodimer/Bcl-3 complexes and facilitates transcriptional repression by p52-c-Rel

RelB: Heterodimers of RelB-p50 or RelB-p52 act as transcriptional activators; does not associate with DNA, p65, or c-Rel; phosphorylation on Thr^{103} and Ser^{573} is followed by proteasomal degradation[15]

c-Rel (Rel): A proto-oncogene involved in differentiation and lymphopoiesis;[16] dimerizes with p65, p50, p52, and itself

Additional information is available from recent reviews.[17-21]

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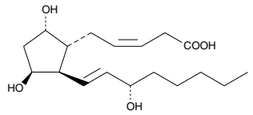
Prostaglandin Receptors

Receptor	Antibodies	Agonists	Antagonists
DP_1	**DP_1 Receptor Polyclonal Antibody** 101640	**PGD_2** 12010, **BW 245C** 12050 **11-keto Fluprostenol** 16783 **15(S)-15-methyl PGD_2** 12730 **15-deoxy-$\Delta^{12,14}$-PGD_2** 12700	**BW A868C** 12060 **AH 6809** 14050 **MK 0524** 10009835 **CAY10471** 10006735
DP_2		**PGD_2** 12010 **15(R) PGD_2** 10118 **15(R)-15-methyl PGD_2** 12720 **11-deoxy-11-methylene-15-keto PGD_2** 12415 **13,14-dihydro-15-keto PGD_2** 12610 **15-deoxy-$\Delta^{12,14}$-PGJ_2** 18570 **PGJ_2** 18500 **15-deoxy-$\Delta^{12,14}$-PGJ_2-2-glycerol** 10010132 **Δ^{12}-PGJ_2** 18550 **15-deoxy-$\Delta^{12,14}$-PGD_2** 12700 **Indomethacin** 70270 **11-keto Fluprostenol** 16783	**BAY-u3405** 10156 **CAY10471** 10006735 **CAY10597** 10012539 **GW 848687X** 10010410 **SC-51089** 10011561 **SC-51322** 10010744
EP_1	**EP_1 Receptor Polyclonal Antibody** 101740	**PGE_2** 14010 **17-phenyl trinor PGE_2** 14810 **17-phenyl trinor 8-*iso* PGE_2** 10007931	**ONO-8711** 14070, **SC-19220** 14060, **AH 6809** 14050, **SC-51089** 10011561, **SC-51322,** 10010744
EP_2 **EP_2**	**EP_2 Receptor Polyclonal Antibody** 101750 **EP_2 Receptor PE Polyclonal Antibody** 10477	**PGE_2** 14010, **Butaprost** 13740 **11-deoxy-16,16-dimethyl PGE_2** 14570 **19(R)-hydroxy PGE_2** 14910 **CAY10408** 13747	**AH 6809** 14050
EP_3	**EP_3 Receptor Polyclonal Antibody** 101760	**PGE_2** 14010 **Sulprostone** 14765 **17-phenyl trinor PGE_2** 14810 **11-deoxy-16,16-dimethyl PGE_2** 14570 **17-phenyl trinor 8-*iso* PGE_2** 10007931	**AH 6809** 14050
EP_4	**EP_4 Receptor (N-Term)** **Polyclonal Antiserum** 101770 **EP_4 Receptor (C-Term)** **Polyclonal Antibody** 101775 **EP_4 Receptor (C-Term)** **Polyclonal PE Antibody** 10479	**PGE_2** 14010 **CAY10580** 16835 **L-902,688** 10007712	**L-161, 982** 10011565 **GW 627368X** 10009162 **AH 23848** 19023
FP	**FP Receptor Polyclonal Antibody** 101802	**$PGF_{2\alpha}$** 16010, **CAY10509** 10009167, **CAY10510** 10009168, **Latanoprost** 16812 **Fluprostenol** 16767, **Bimatoprost** 16820 **Cloprostenol** 16764 **15(S)-15-methyl-$PGF_{2\alpha}$** 16743 **Tafluprost** 10005440	**AL 8810** 16735, **AL 8810 isopropyl ester** 10113 **$PGF_{2\alpha}$ dimethyl amide** 16032 **$PGF_{2\alpha}$ dimethyl amine** 16033
IP	**IP Receptor (murine)** **Polyclonal Antibody** 160070 **IP Receptor (human)** **Polyclonal Antibody** 10005518	**PGI_2** 18220, **MRE-269** 10010412 **Iloprost** 18215 **Beraprost** 18230, **NS-304** 10010411 **13,14-dehydro-15-cyclohexyl** **Carbaprostacyclin** 18212, **Ciprostene** 18216 **Carbaprostacyclin** 18210 **Treprostinil** 10162	**CAY10441** 10005186, **CAY10449** 10005913
TP	**TP Receptor (human) Polyclonal** **FITC Antibody** 10012559 **TP Receptor (human)** **Polyclonal Antibody** 10004452 **TP Receptor (murine)** **Polyclonal Antibody** 101882	**U-46619** 16450 **Carbocyclic TXA_2** 19010 **I-BOP** 19600, **U-44069** 16440	**SQ 29,548** 19025, **BAY-u3405** 10156 **I-SAP** 19021, **Pinane TXA_2** 19020 **CAY10471** 10006735, **GW 627368X** 10009162 **BM 567** 10155, **CAY10535** 10010396, **AH 23848** 19023
BLT_1	**BLT_1 Receptor Polyclonal Antiserum** 100019 **BLT_1 Receptor Monoclonal Antibody** 120111 **BLT_1 Receptor Polyclonal Antibody** 120114	**LTB_4** 20110 **20-trifluoro LTB_4** 20195	**U-75302** 70705, **LY223982** 10010024 **LTB_4 Ethanolamide** 20112 , **14,15-dehydro LTB_4** 20150 **LY293111** 10009768
BLT_2	**BLT_2 Receptor Polyclonal Antibody** 120124	**LTB_4** 20110	**LY255283** 70715
$CysLT_1$	**$CysLT_1$ Receptor Polyclonal Antibody** 120500	**LTC_4** 20210, **LTD_4** 20310, **LTE_4** 20410	**MK 571 (sodium salt)** 70720 **BAY-u9773** 70770, **Zafirlukast** 10008282 **Montelukast** 10008318, **Pranlukast** 10008319 **LY171883** 70710
$CysLT_2$	**$CysLT_2$ Receptor (C-Term)** **Polyclonal Antibody** 120550 **$CysLT_2$ Receptor (N-Term)** **Polyclonal Antibody** 120560	**LTC_4** 20210, **LTD_4** 20310, **LTE_4** 20410	**BAY-u9773** 70770

2,3-dinor-11β-Prostaglandin $F_{2\alpha}$ 16530

[240405-20-3]
MF: $C_{18}H_{30}O_5$ **FW:** 326.4 **Purity:** ≥98%*
A solution in ethanol **Stability:** ≥1 year at -20°C
Summary: Key urinary metabolite of PGD_2; represents approximately 1% and 4% of the infused radiolabeled dose in monkeys and humans, respectively

25 µg
50 µg
100 µg
500 µg

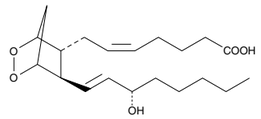


•Also Available: **2,3-dinor-11β-Prostaglandin $F_{2\alpha}$ Lipid Maps MS Standard** (10007225)

Prostaglandin H_2 17020

[42935-17-1]
MF: $C_{20}H_{32}O_5$ **FW:** 352.5 **Purity:** ≥95%*
A solution in acetone **Stability:** ≥6 months at -80°C
Summary: A COX metabolite of arachidonic acid and precursor for all 2-series PGs and TXs; acts as a TP receptor agonist and suicide substrate for TX synthase (K_i = 18 µM)

25 µg
50 µg
100 µg
500 µg

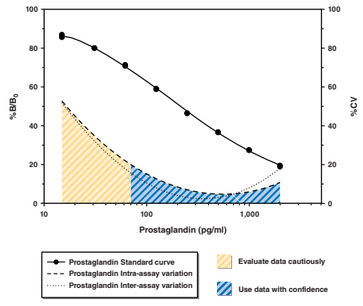


•Also Available: **Prostaglandin H_2 Lipid Maps MS Standard** (10007231)

Prostaglandin Screening EIA Kit 514012

Stability: ≥1 year at -20°C
Sensitivity: 50% B/B_0: 220 pg/ml • 80% B/B_0: 30 pg/ml
Summary: This assay was developed for screening applications in which the relative amount of PG production for a large number of cell culture samples must be determined. The antiserum used in this assay exhibits high cross reactivity for most PGs which will allow quantification of all the PGs in a given sample with a single assay.

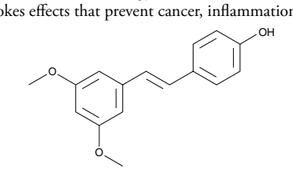
96 solid/strip wells
480 solid/strip wells



Pterostilbene 13000

[537-42-8] 3',5'-Dimethoxy-4-Stilbenol, trans-3,5-Dimethoxy-4'-Hydroxystilbene
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

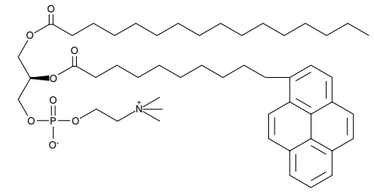
50 mg
100 mg
250 mg
500 mg



10-Pyrene-PC 62245

[95864-17-8] 1-Palmitoyl-2-pyrenedecanoylphosphatidylcholine
MF: $C_{50}H_{76}NO_8P$ **FW:** 850.1 **Purity:** ≥98%
A solution in chloroform **Stability:** ≥1 year at -20°C
Summary: A fluorogenic substrate for all PLA_2s with the exception of $cPLA_2$ and PAF-AH

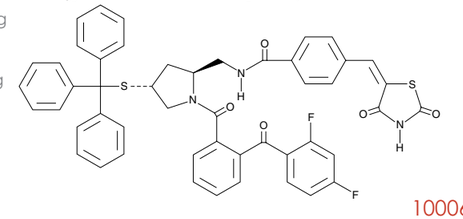
1 mg
5 mg
10 mg
25 mg



Pyrrophenone 13294

[341973-06-6]
MF: $C_{49}H_{37}F_2N_3O_5S_2$ **FW:** 850.0 **Purity:** ≥90%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: Reversible, selective inhibitor of $cPLA_2$ with an IC_{50} value of 4.2 nM in enzyme assays; potently blocks the release of AA and the production of PGE_2 and LTC_4 in cells (IC_{50} = 24, 25, and 14 nM, respectively)

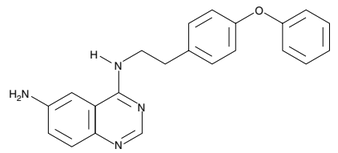
500 µg
1 mg
5 mg
10 mg



QNZ 10006734

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

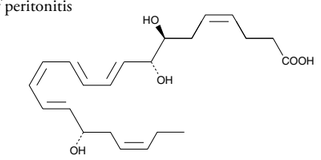
500 µg
1 mg
5 mg
10 mg



Resolvin D1 10012554

[872993-05-0] 17(S)-Resolvin D1, RvD1
MF: $C_{22}H_{32}O_5$ **FW:** 376.5 **Purity:** ≥95%
A solution in ethanol **Stability:** ≥1 year at -80°C
Summary: A potent anti-inflammatory mediator derived physiologically from the sequential oxygenation of DHA by 15- and 5-LO; reduces human leukocyte transendothelial migration (EC_{50} = ~30 nM) and limits leukocyte infiltration in a mouse model of peritonitis

10 µg
25 µg
50 µg
100 µg

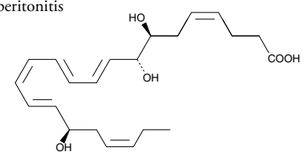


**All 5-cis 2-series PGs (those containing a 5,6-double bond) will contain a small amount of the 5-trans isomer. This isomer is generally undetectable using normal phase silica columns and plates, but may be resolved using RP-HPLC. The purity for all such 2-series PGs excludes the 1-3% trans isomer which will generally be present.*

17(R)-Resolvin D1 13060

[528583-91-7] Aspirin-triggered-Resolvin D1, AT-RvD1, 17(R)-RvD1
MF: $C_{22}H_{32}O_5$ **FW:** 376.5 **Purity:** ≥95%
A solution in ethanol **Stability:** ≥1 year at -80°C
Summary: An aspirin-triggered epimer of RvD1; reduces human leukocyte transendothelial migration (EC_{50} ~30 nM), and limits leukocyte infiltration in a murine model of peritonitis

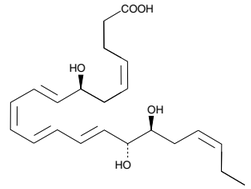
10 µg
25 µg
50 µg
100 µg



Resolvin D2 10007279

[810668-37-2] 7(S),16(R),17(S)-Resolvin D2
MF: $C_{22}H_{32}O_5$ **FW:** 376.5 **Purity:** ≥95%
A solution in ethanol **Stability:** ≥1 year at -80°C
Summary: Dampens excessive neutrophil trafficking to sites of inflammation; reduces neutrophil infiltration by 70% at doses as low as 10 pg per mouse and significantly reduces leukocyte adherence and emigration at 1 nM

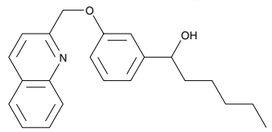
10 µg
25 µg
50 µg
100 µg



REV 5901 70600

[101910-24-1]
MF: $C_{22}H_{25}NO_2$ **FW:** 335.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥1 year at Room temperature
Summary: Antagonist of CysLT receptors with a K_i value of 0.7 µM for guinea pig lung membranes; inhibits rat neutrophil 5-LO (IC_{50} = 0.12 µM)

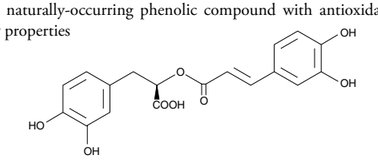
5 mg
10 mg
50 mg
100 mg



Rosmarinic Acid 70900

[20283-92-5]
MF: $C_{18}H_{16}O_8$ **FW:** 360.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥1 year at Room temperature
Summary: A naturally-occurring phenolic compound with antioxidant and anti-inflammatory properties

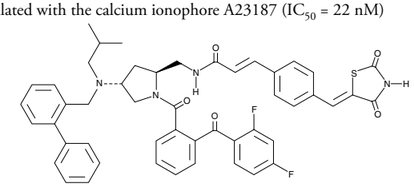
5 mg
10 mg
50 mg
100 mg



RSC-3388 13343

[337307-06-9]
MF: $C_{49}H_{44}F_2N_4O_5S$ **FW:** 839.0 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A pyrrolidine derivative that potently inhibits cPLA$_2$α, suppressing both recombinant human cPLA$_2$ *in vitro* (IC_{50} = 1.8 nM) and cellular PLA$_2$ activity in cells stimulated with the calcium ionophore A23187 (IC_{50} = 22 nM)

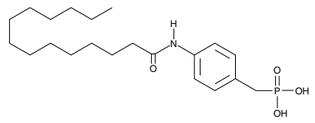
500 µg
1 mg
5 mg
10 mg



S32826 13664

[1096770-84-1]
MF: $C_{21}H_{36}NO_4P$ **FW:** 397.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent and selective inhibitor of autotaxin, inhibiting recombinant autotaxin β with an IC_{50} value of 8.8 nM; inhibits LPA release from adipocytes (IC_{50} = 90 nM) and reduces plasma autotaxin activity by 57% when used at 5 µM

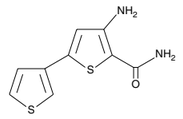
1 mg
5 mg
10 mg
25 mg



SC-514 10010267

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

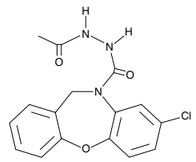
5 mg
10 mg
25 mg
50 mg



SC-19220 14060

[19395-87-0]
MF: $C_{16}H_{14}ClN_3O_3$ **FW:** 331.8 **Purity:** ≥96%
A crystalline solid **Stability:** ≥1 year at -20°C
Summary: A selective EP$_1$ receptor antagonist; displaces radiolabeled PGE$_2$ from the cloned human EP$_1$ receptor with an IC_{50} value of 6.7 µM; exhibits no binding at the human EP$_2$ receptor

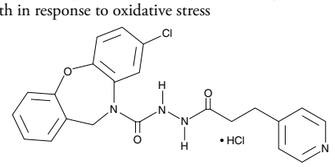
1 mg
5 mg
10 mg
25 mg



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

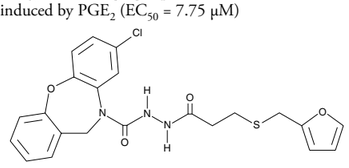
1 mg
5 mg
10 mg
25 mg



SC-51322 10010744

[146032-79-3]
MF: $C_{22}H_{20}ClN_3O_4S$ **FW:** 457.9 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A selective EP$_1$ antagonist that inhibits PGE$_2$ signaling in a guinea pig ileum muscle strip assay (pA$_2$ =8.1); demonstrates analgesic activity in a mouse writhing assay (ED_{50} = 0.9 mg/kg); potentiates the vasorelaxation of human pulmonary vein induced by PGE$_2$ (EC_{50} = 7.75 µM)

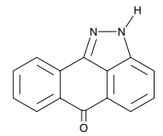
1 mg
5 mg
10 mg
25 mg



SP 600125 10010466

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

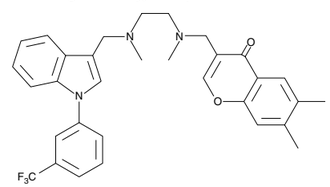
5 mg
10 mg
25 mg
50 mg



SPD-304 10008012

[869998-49-2]
MF: $C_{32}H_{32}F_3N_3O_2$ **FW:** 547.6 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A TNFR1 antagonist (IC_{50} = 22 µM)

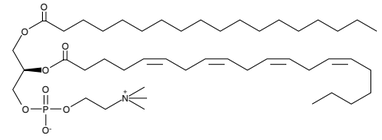
500 µg
1 mg
5 mg
10 mg



1-Stearoyl-2-Arachidonoyl PC 10009864

[35418-59-8] SAPC, 1-Stearoyl-2-Arachidonoyl Phosphatidylcholine
MF: $C_{46}H_{84}NO_8P$ **FW:** 810.1 **Purity:** ≥98%
A solution in ethanol **Stability:** ≥1 year at -20°C
Summary: Preferred phospholipid substrate for cPLA$_2$; an important source of activation-induced arachidonate released as a substrate for COX-2 mediated signaling

1 mg
5 mg
10 mg
25 mg

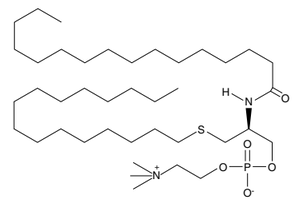


•Also Available: **1-Stearoyl-2-Arachidonoyl PC-d$_4$** (10009431)

Thioetheramide-PC 62750

[116457-99-9]
1-Palmitylthio-2-palmitoylamido-1,2-dideoxy-sn-glycero-3-phosphorylcholine
MF: $C_{40}H_{83}N_2O_5PS$ **FW:** 735.1 **Purity:** ≥95%
A solution in ethanol **Stability:** ≥1 year at -20°C
Summary: A competitive, reversible inhibitor of sPLA$_2$ (IC_{50} = 2 µM at a substrate concentration of 0.5 mM)

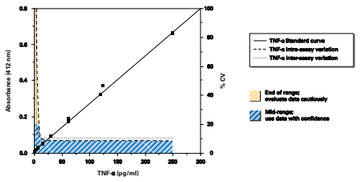
1 mg
5 mg
10 mg
25 mg



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 (*i.e.* 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.

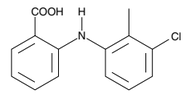
96 wells
480 wells



Tolfenamic Acid 70480

[13710-19-5] Clotam
MF: $C_{14}H_{12}ClNO_2$ **FW:** 261.7 **Purity:** ≥99%
A crystalline solid **Stability:** ≥1 year at Room temperature
Summary: An NSAID thought to exert its actions by a prostanoid-independent mechanism; inhibits fMLP- and A23187-induced Ca^{2+} influx in human neutrophils with an IC_{50} value of approximately 20 µM

5 g
10 g
25 g
50 g



Toll-Like Receptor 2 Monoclonal Antibody (Clone TL2.1) 13587

Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: CHO cells transfected with human TLR2 cDNA • Host: mouse, clone TL2.1 • Cross Reactivity: (+) human and canine TLR2 • Application(s): FC (intracellular and cell surface), ICC, IHC, IP, and WB • TLR2 is differentially expressed in human cells. Historically speaking, TLR expression has been most extensively studied in the immune system. Overall, TLRs are highly expressed in immune competent cells, including macrophages, dendritic cells, neutrophils, mucosal epithelial cells, and dermal endothelial cells. However, TLRs have also been identified in many other cell types and anatomical tissue locations where they are expressed either constitutively or induced during infection.

1 ea

Toll-Like Receptor 4 Monoclonal Antibody (Clone HTA125) 13589

Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: Ba/F3 cell line expressing human TLR4 cell surface antigen • Isotype: IgG_{2aK} • Host: mouse, clone HTA125 • Cross Reactivity: (+) human and canine TLR4 • Application(s): FC (intracellular and cell surface), ICC, IP, and neutralization • TLR4 serves as the main mediator of LPS signaling that leads to NF-κB activation.

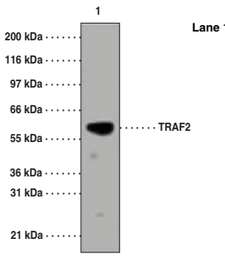
1 ea

•Also Available: **Toll-Like Receptor 1 Polyclonal Antibody** (13582)
Toll-Like Receptor 3 Monoclonal Antibody (Clone 40C1285.6) (13588)
Toll-Like Receptor 5 Monoclonal Antibody (Clone 85B152.5) (13595)
Toll-Like Receptor 7 Polyclonal Antibody (13591)
Toll-Like Receptor 8 Monoclonal Antibody (Clone 44C143) (13592)
Toll-Like Receptor 9 Monoclonal Antibody (Clone 26C593.2) (13593)
Toll-Like Receptor 10 Monoclonal Antibody (Clone 158C1114) (13584)
Toll-Like Receptor 11 Polyclonal Antibody (13585)
Toll-Like Receptor 12 Polyclonal Antibody (13586)

TRAF2 Monoclonal Antibody (Clone 33A1293) 10855

Protein G-purified IgG **Stability:** ≥6 months
Summary: Antigen: fusion protein corresponding to amino acids 205-222 of human TRAF2 • Host: mouse • Cross Reactivity: (+) human TRAF2 • Application(s): WB • TRAFs form a family of cytoplasmic adapter proteins that mediate signal transduction from many members of the TNF-R superfamily (*e.g.*, RANK, CD30, CD40, *etc.*) and the interleukin-1 receptor. TRAF2 is a 501-amino acid protein involved in cellular resistance to TNF-induced apoptosis.

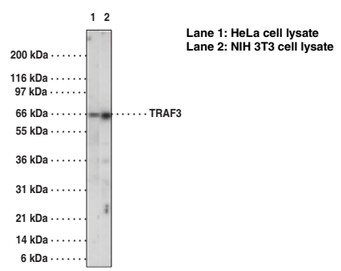
100 µg



TRAF3 Polyclonal Antibody 10872

Protein G-purified IgG **Stability:** ≥6 months at -20°C
Summary: Antigen: peptide corresponding to amino acids 323-340 of human TRAF3 • Host: rabbit • Cross Reactivity: (+) human and mouse TRAF3 • Application(s): WB • TRAFs form a family of cytoplasmic adapter proteins that mediate signal transduction from many members of the TNF-R superfamily (*e.g.*, RANK, CD30, CD40, *etc.*) and the IL-1 receptor. TRAF3, originally named CRAF1, interacts directly with the CD40 cytoplasmic tail through a region of similarity to the TRAFs.

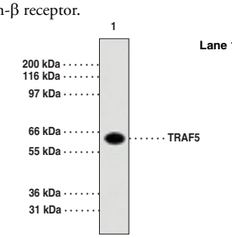
1 ea



TRAF5 Monoclonal Antibody (Clone 55A219) 10873

Protein G-purified IgG **Stability:** ≥6 months at -20°C
Summary: Antigen: fusion protein corresponding to amino acids 77-186 of human TRAF5 • Host: mouse • Cross Reactivity: (+) human and mouse TRAF5 • Application(s): WB • Human TRAF5 is a 557-amino acid protein that is implicated in NF-kB and c-Jun NH(2)-terminal kinase/stress-activated protein kinase activation by members of the TNF receptor superfamily, including CD27, CD30, CD40, and lymphotoxin-β receptor.

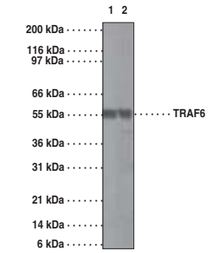
1 ea



TRAF6 Polyclonal Antibody 10874

Protein G-purified IgG **Stability:** ≥6 months at -20°C
Summary: Antigen: peptide corresponding to amino acids 436-449 of human TRAF6 • Host: rabbit • Cross Reactivity: (+) human and mouse TRAF6 • Application(s): WB • TRAF6 plays critical roles in perinatal and postnatal survival, bone metabolism, LPS, and cytokine signaling.

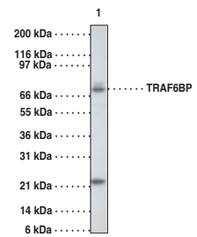
1 ea



TRAF6BP Polyclonal Antibody 10894

T6BP, TAX1-binding protein, TAX1BP1, TRAF6 Binding Protein
Summary: Antigen: peptide corresponding to amino acids 718-735 of human TRAF6BP • Host: rabbit • Cross Reactivity: (+) human TRAF6BP • Application(s): WB • A TRAF-interacting protein that associates with TRAF6. T6BP shares an overall 50% identity and 59% similarity to chicken protein MDP62, which has been implicated in promoting neurite outgrowth. T6BP-TRAF6 complex formation is dependent on the presence of the IRAK.

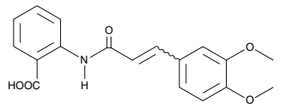
1 ea



Tranilast 13044

[53902-12-8] N-(3',4'-dimethyoxycinnamoyl)-Anthranilic Acid, MK 341, Rizaben, SB 252218, Tranpro
MF: $C_{18}H_{17}NO_5$ **FW:** 327.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: Inhibits the production or release of chemical mediators and cytokines from inflammatory cells and macrophages and interferes with the proliferation and migration of vascular medial smooth muscle cells

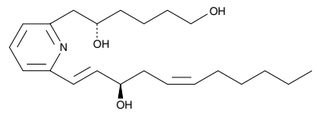
1 mg
5 mg
10 mg
50 mg



U-75302 70705

[119477-85-9]
MF: $C_{22}H_{35}NO_3$ **FW:** 361.5 **Purity:** ≥98%
A solution in ethanol **Stability:** ≥2 years at -20°C
Summary: A BLT_1 receptor antagonist with a K_i value of 159 nM on guinea pig lung membranes; does not antagonize the binding of $[^3H]$-LTB_4 to the human BLT_2 receptor

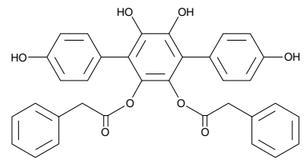
50 µg
100 µg
500 µg
1 mg



Vialinin A 10010519

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

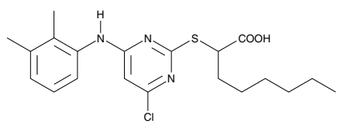
1 mg
5 mg
10 mg
25 mg



YS121 13665

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

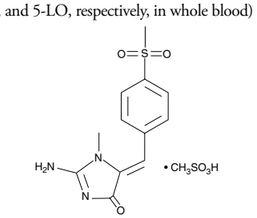
1 mg
5 mg
10 mg
25 mg



ZLJ-6 13271

[1051931-39-5]
MF: CH_4SO_3 • CH_3SO_3H **FW:** 375.4 **Purity:** ≥98%
Supplied as: A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A dual inhibitor of COX and 5-LO enzymes (IC_{50} = 0.73, 0.31, and 0.99 µM for COX-1, COX-2, and 5-LO, respectively, in whole blood)

1 mg
5 mg
10 mg
25 mg



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