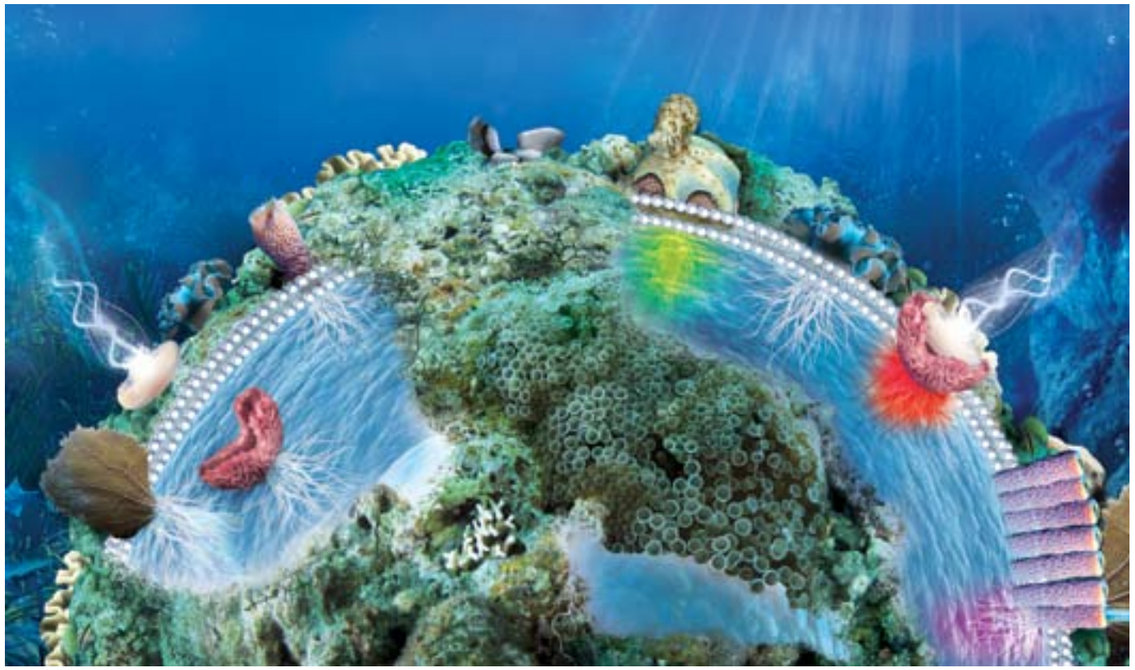

RECEPTOR SIGNALING
Cayman
CHEMICAL

Thomas G. Brock, Ph.D.

Introduction to

Receptor Signaling



Effective communication is crucial for success. Whether you are a graduate student, a postdoc, or a professor, it is absolutely essential that you can get your messages sent, received, and understood. This is the backbone of a research career: the creation of novel concepts, transposing the thoughts into signals encoded in speech and text, and delivering them to receptive audiences near and far. Failure to communicate sufficiently can be disastrous.

This is how it is with cells, too. They must sense the changing world around them, process those perceptions appropriately, and respond with signals of their own. Each cell is awash in a sea of potential cues. The challenge is, by displaying appropriate receptors, to recognize the important signals and integrate their messages into the proper response. Failure to do so can result in death or disease.

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abbreviations

cAMP	Cyclic Adenosine Monophosphate
ATP	Adenosine-5′-Triphosphate
COX	Cyclooxygenase
CysLT	Cysteinyl Leukotriene
EC_{50}	Effective Concentration
EGF	Epidermal Growth Factor
FC	Flow Cytometry
FEGF	Fibroblast Growth Factor
GPCR	G Protein-Coupled Receptor
cGMP	Cyclic Guanosine Monophosphate
GSK	Glycogen Synthase Kinase
IC_{50}	Inhibitory Concentration
ICC	Immunocytochemistry
IHC	Immunohistochemistry
IP	Immunoprecipitation
LT	Leukotriene
NF-κB	Nuclear Factor-κB
iNOS	Nitric Oxide Synthase
PAF	Platelet-Activating Factor
PDE	Phosphodiesterase
PDGF	Platelet-Derived Growth Factor
PG	Prostaglandin
PI	Phosphatidylinositol
PI3K	Phosphoinositide 3-Kinase
PtdIns	Phosphatidylinositol
PTEN	Phosphatase and Tensin Homolog
RNA	Ribonucleic Acid
Ser	Serine
TGF	Tumor Growth Factor
Thr	Threonine
mTOR	Mammalian Target of Rapamycin
VEGF	Vascular Endothelial Growth Factor
WB	Western Blot

vol. 15 Rs

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The Many Faces of PI3K

Phosphoinositide 3-kinase (PI3K) takes center stage in many discussions regarding cancer and diabetes, but, in reality, it is much more complex than simply being a pivotal player in these and other diseases. First, it is a multimeric enzyme, and its subunits have distinctive characteristics. Second, like other kinases, PI3K is involved in a wide variety of signaling pathways. Both sides of PI3K deserve attention.

The Regulatory Subunits of PI3K (human)

PI3K is usually described as a heterodimer consisting of an 85 kD regulatory subunit (p85) and a 110 kD catalytic subunit (p110). In this model, which pertains to the Class IA PI3Ks, the regulatory subunit inhibits the activity of the catalytic subunit in resting cells. In stimulated cells, the p85-p110 dimer is recruited to activated receptors or adaptor molecules. The p85-mediated inhibition of catalytic activity is released and the enzyme is brought in contact with its lipid substrate in the membrane, leading to the phosphorylation of some form of phosphatidylinositol at the 3' position. Distinct genes encode the subunits of the Class IA PI3Ks, including 2 regulatory proteins, p85α and β, and 3 catalytic subunits, p110α, β, and δ. Four more genes encode additional regulatory proteins ranging in size from 55 to 150 kD and five genes give other catalytic enzymes of the less well-known Class IB, II, and III PI3Ks (see Table).

Class	Catalytic Subunit	Regulatory Subunit
IA	p110α p110β p110δ	p85α, p85β, p55γ
IB	p110γ	p84, p101
II	pI3KC2α pI3KC2β pI3KC2γ	(none)
III	Vps34	p150 (Vps15)

While the catalytic portion of PI3K may do the work, it is the regulatory subunit which determines when and where it acts. The best known regulatory subunit is p85α, which, with p110, is usually located adjacent to a receptor tyrosine kinase, including many growth factor receptors. When the receptor is activated and autophosphorylated, p85 binds the phosphorylated receptor through its two SH2 domains and its p110 catalytic partner (p110α, β, or δ) can act at the plasma membrane. p85α also has an amino-terminal SH3 domain, which mediates additional protein interactions, as well as a Rho-GAP domain, which can activate GTPases like Rab. p85α can reportedly be phosphorylated on serines 154 and 608 and on tyrosines 452, 467, 508, 556, 580, and 607, as well as acetylated on Lys530. In addition to associating with receptors for EGF, VEGF, PDGF, SCF (KIT), FGF, NGF, and insulin, p85α binds CD28, c-Abl, Grb2, Shb, Shc1, and XBP-1. It is involved in such diverse processes as growth factor signaling, insulin-stimulated glucose uptake and glycogen synthesis in insulin-sensitive tissues, T cell co-stimulation, leukocyte migration, and blood coagulation. Four alternatively-spliced isoforms have been described; the truncated isoform 2 is expressed in skeletal muscle, brain, kidney, and cardiac muscle.

p85β also associates with p110α, β, or δ. Like p85α, it has two SH2 domains, an SH3 domain, and a Rho-GAP domain. It can be phosphorylated on serines 262 and 263 as well as tyrosines 365, 464, 467, and 605. p85β binds with the receptors EGFR, FGFR, VEGFR, IGF1R, KIT, AXL, and CSF1R and interacts with IRS-1, CD28, Socs1, Fyn, Hck, and Grb2. In addition to growth factor and insulin

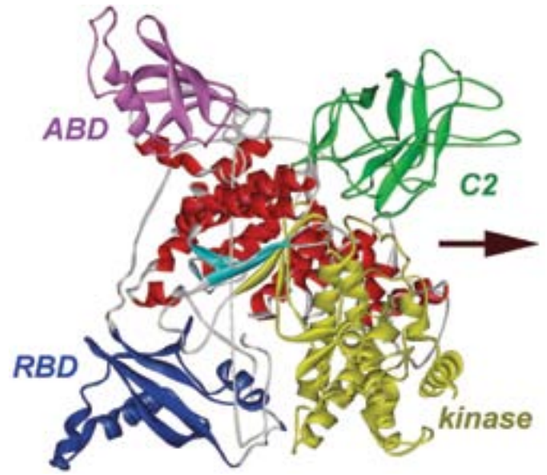

Figure 1. Structure of p110α. ABD, adaptor binding domain; RBD, Ras binding domain

receptor signaling, leukocyte migration, blood coagulation, and T cell co-stimulation, p85β modulates apoptosis and small GTPase-mediated signal transduction.

Other PI3K regulatory subunits include p55γ, p84 (p87PIKAP), p101 (FOAP-2), and Vps15 (p150). p55γ is similar to p85α and β, in that it binds the same catalytic subunits and modulates similar processes, but differs by being restricted in distribution, with highest levels in brain and testis. Also, p55γ has two SH2 binding domains, but lacks the SH3 and Rho-GAP domains of p85α and β. p84 and p101 are regulatory subunits for the Class Ib p110γ catalytic protein. p84 interacts with the heterotrimeric G protein Gβγ and the phosphodiesterase PDE3B, as well as p110γ. p101 is most abundant in leukocytes, spleen and lymph nodes. Both p84 and p101 lack SH2, SH3, and Rho-GAP domains and seem to be involved primarily in platelet activation and blood coagulation.

The p150 regulatory protein, also known as vacuolar protein sorting

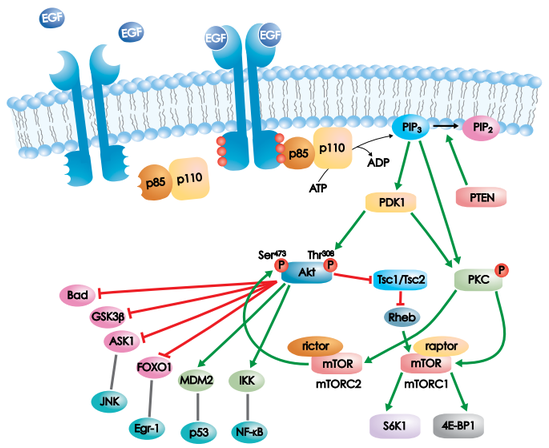

Figure 2. Signaling through EGFR/PI3K/Akt

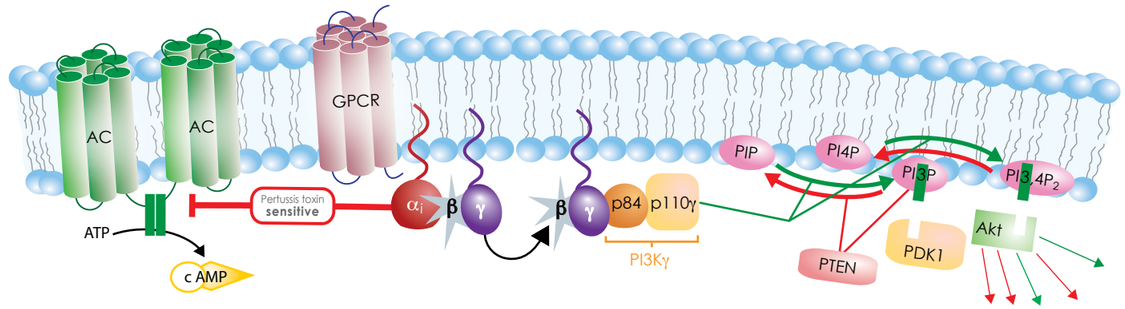

Figure 3. Signaling through GPCR/PI3Kγ/Akt

15 (Vps15), binds the Class III PI3K Vps34. Interestingly, p150 has kinase activity. Structurally, p150 contains several WD domains, for protein binding, and HEAT domains, which are involved in intracellular trafficking. It is myristoylated, which serves to position the p150/Vps34 dimer on the surface of endosomal membranes. Together, they modulate endocytic trafficking and autophagy.[2]

The Catalytic Subunits of PI3K (human)

The catalytic subunits of Class IA PI3Ks include p110α, β, and δ. Each contains an N-terminal adaptor binding domain (ABD), a Ras binding domain (RBD), a C2 domain, a helical domain (HD), and a catalytic kinase domain (Figure 1). C2 domains often mediate calcium-dependent lipid binding, but this PI3K-type C2 domain does not bind calcium. The C2 and kinase domains (at right) are thought to orient toward the membrane.[3] The Class IB p110γ has a similar layout. Class IA and IB subunits can use PI, PI-4-phospate (PI-4-P), and PI-4,5-P_2 as substrates to produce PI-3-P, PI-3,4-P_2, and PI-3,4,5-P_3, respectively.

Mutations in p110α increase the interaction of this subunit with HRA1/KRAS and contribute to various types of cancer, including forms of breast, colorectal, gastric, non-small cell lung, ovarian and hepatocellular cancers.[4] Mutations in p110α are also linked to nevus (pigmented mole) formation. Interestingly, there is little evidence for roles for mutations in p110β, δ, or γ in cancer. Experiments using IC-87114, a selective p110δ inhibitor, suggest a role for this PI3K in allergic responses. The restricted distribution of p110γ to cells within the vascular and lymphoid systems implies that it may be modulated therapeutically to control inflammation.

The Class II PI3Ks, PI3KC2α, β, and γ, share the RBD, PI3K-type C2, and catalytic domains of Class I PI3Ks. Each also has a second C2 domain, which binds divalent cations like calcium, and a phox (PX) homology domain, involved in PI binding. These catalytic subunits do not bind regulatory subunits. Instead, they are activated by divalent cations and protein interactions. PI3KC2α functions with Ca^{2+} or Mg^{2+} and binds ERBB2 or clathrin. PI3KC2β uses Ca^{2+}, Mg^{2+}, or Mn^{2+} and interacts with ERBB2, GRB2, and SHC1. Less is known about PI3KC2γ. All three Class II PI3Ks phosphorylate PI and PI-4-P, but not PI-4,5-P_2. Thus, they make PI-3-P and PI-3,4-P_2, but not PI-3,4,5-P_3.

The Class III PI3K Vps34 (PI3K type 3) lacks ABD and RBD, featuring primarily the PI3K-type C2 and kinase domains. With Mn^{2+} as a cofactor and p150 as a regulatory component, Vps34 catalyzes only the conversion of PI to PI-3-P. Vps34 complexes with Beclin-1 and either UVRAG or Ambra1 to modulate autophagy. Also, Vps34/p150 directly activates TORC1 in response to either glucose or amino acids.

PI3K in EGF Signaling

The PI3K/Akt pathway is central to many forms of cancer. The signaling pathway initiated by EGF through EGFR and p85α/p110α is prototypical (Figure 2). Binding of EGF to individual EGFR subunits causes receptor dimerization and autophosphorylation, followed by recruitment of p85α/p110α to the receptor (see related article on page 12). The binding of p85α to EGFR suppresses inhibition of p110α by p85α, allowing p110α to phosphorylate PIP_2. If this reaction is not reversed by the phosphatase PTEN, then PIP_3 can activate a large number of proteins, including PDK1 and PKC. PDK1 phosphorylates Thr^{308} on Akt, resulting in partial activation. PKC activates mTOR, and mTOR associated with Rictor in mTORC2 phosphorylates Ser^{473} on Akt, fully activating it. Akt phosphorylates Tsc2 of the Tsc1/Tsc2 complex, removing its inhibitory effects on Rheb and mTORC1, activating mTORC1, which drives growth through S6K1 and 4E-BP1. Activated Akt phosphorylates several proteins, altering various pathways linked to cancer. For example, it reduces apoptosis by inhibiting Bad, a pro-apoptotic Bcl-2 family member, and by blocking ASK1 signaling through the JNK pathway. Suppression of GSK3β, a kinase which modulates multiple pathways, and FOXO1, which reduces expression of the transcription factor early growth response 1 (Egr-1), affects cell proliferation and survival. Akt increases Mdm2-mediated ubiquitination and degradation of the tumor suppressor p53 and induces IκB kinase (IKK) to initiate NF-κB-mediated expression of anti-apoptotic genes. Thus, the EGFR/PI3K/Akt pathway, amplified through mTOR, controls many pathways relevant to cancer.

PI3K in GPCR Signaling

The savvy cell biologist knows that GPCR are seven transmembrane proteins that associate with heterotrimeric G proteins. Most also know that, of the α, β, and γ G proteins, the Gα subunit determines the type of second messenger employed following receptor activation. For example, when GDP in the $G\alpha_i$ subunit is replaced with GTP, it dissociates from the GPCR, releasing the Gβγ dimer, to trigger the $G\alpha_i$-specific pathway, the inhibition of adenylate cyclase-mediated cAMP production (Figure 3). However, it is the receptor aficionado who knows that the Gβγ dimer can evoke a distinct signal. By recruiting the PI3K regulatory subunits p84 and p101 to the membrane, Gβγ initiates PIP_3 production through p110γ activity.[5] Gβγ signaling through PI3Kγ is featured in leukocytes.

References

1. Chamberlain, M.D., Berry, T.R., Pastor, M.C. , *et al. J. Biol. Chem.* **279(47),** 48607-48614 (2004).
2. Backer, J.M. *Biochem. J.* **410,** 1-17 (2008).
3. Huang, C.-H., Mandelker, D., Schmidt-Kittler, O., *et al. Science* **318,** 1744-1748 (2007).
4. Yuan, T.L. and Cantley, L.C. *Oncogene* **27,** 5497-5510 (2008).
5. Suire, S., Coadwell, J., Ferguson, G.J., *et al. Curr. Biol.* **15,** 566-570 (2005).

PI3 Kinase/Akt Signaling

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

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

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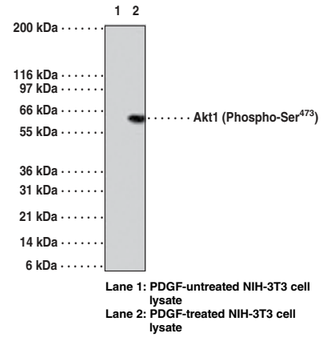

Akt1 Polyclonal Antibody 13732

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

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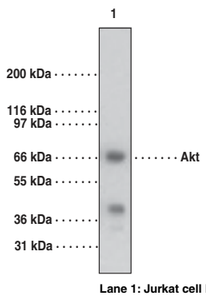

•Also Available: **Akt (human recombinant) Western Ready Control** (10010079)

Akt2 Monoclonal Antibody(Clone 95C567.1.2) 13734

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

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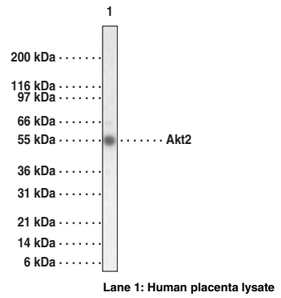
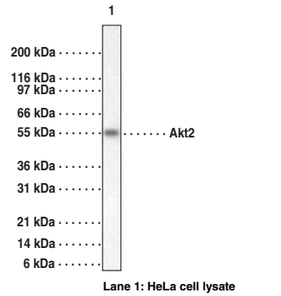


Akt2/3 Polyclonal Antibody 13735

Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human Akt2 amino acids 319-331; this sequence is 100% homologus in Akt3 • Host: rabbit • Cross Reactivity: (+) human Akt2/3 • Application(s): WB • Akt/PKB is a Ser/Thr kinase involved in some human cancers and an important signaling molecule in the insulin signaling pathway. There are three known isoforms of this enzyme in mammalian cells (1, 2, and 3).

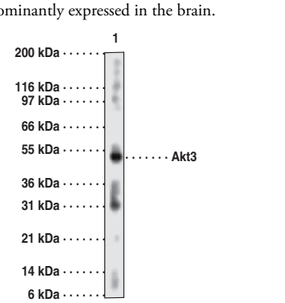
1 ea



Akt3 Monoclonal Antibody (Clone 66C1247.1) 13736

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

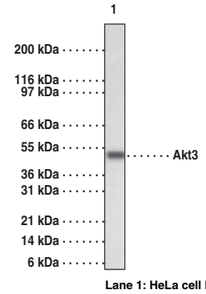
1 ea



Akt3 Polyclonal Antibody 13737

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

1 ea



AS-041164 13622

[1146702-72-8]
MF: $C_{11}H_7NO_4S$ **FW:** 249.2 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent inhibitor of PI3K with selectivity for the class IB isoform PI3Kγ (IC_{50} = 70 nM), compared to PI3Kα (IC_{50} = 240 nM), PI3Kβ (IC_{50} = 1.45 µM), and PI3Kδ (IC_{50} =1.70 µM); shows little or no activity against 38 other common kinases

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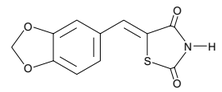

AS-252424 10009052

[900515-16-4]
MF: $C_{14}H_8FNO_4S$ **FW:** 305.3 **Purity:** ≥95%
A crystalline solid **Stability:** ≥1 year at -20°C
Summary: A potent inhibitor of PI3K with selectivity for the γ isoform; inhibits human recombinant PI3Kγ, α, β, and δ with IC_{50} values of 30, 940, 20000, and 20000 nM, respectively

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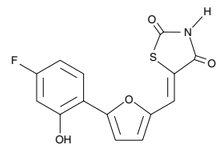

AS-604850 10010175

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

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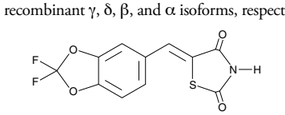

AS-605240 10007707

[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 PI3K γ that suppresses joint inflammation in mouse 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

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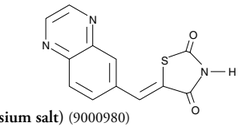
10 mg
50 mg

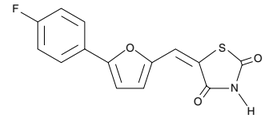


•Also Available: **AS-605240 (potassium salt)** (9000980)

CAY10505 10009078

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

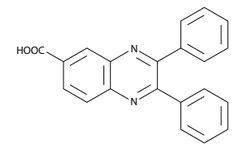
5 mg
10 mg
25 mg
50 mg



CAY10567 10010233

[32387-96-5] BML-257
MF: $C_{21}H_{14}N_2O_2$ **FW:** 326.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An inhibitor of Akt1 translocation that also inhibits hepatitis C virus (HCV) NS5B RNA-dependent RNA polymerase (RdRp) (IC_{50} = 79 µM)

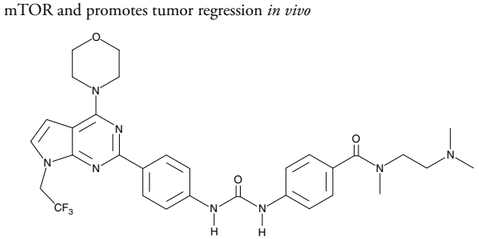
100 mg
250 mg
500 mg
1 g



CAY10626 13838

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

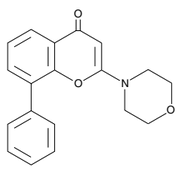
1 mg
5 mg
10 mg
25 mg



LY294002 70920

[154447-36-6]
MF: $C_{19}H_{17}NO_3$ **FW:** 307.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥1 year at -20°C
Summary: A selective PI3K inhibitor with an IC_{50} value of 1.4 µM

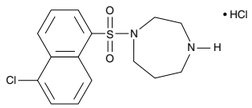
5 mg
10 mg
25 mg
50 mg



ML-9 10010236

[105637-50-1]
MF: $C_{15}H_{17}ClN_2O_2S$ • HCl **FW:** 361.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An inhibitor of PKB/Akt activity (IC_{50} = 10-50 µM) that inhibits insulin-stimulated glucose transport and intracellular protein translocation; inhibits additional Ser/Thr kinases including PKA (IC_{50} = ~20 µM), p90 S6 (IC_{50} = ~50 µM), and MAP kinase (IC_{50} = ~35 µM)

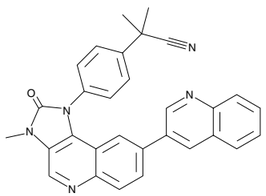
10 mg
50 mg
100 mg
250 mg



NVP-BEZ235 10565

[915019-65-7]
MF: $C_{30}H_{23}N_5O$ **FW:** 469.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent dual inhibitor of PI3K and mTOR that is well tolerated, displays disease stasis when administered orally, and enhances the efficacy of other anti-cancer agents when used in *in vivo* combination studies; inhibits PI3K isoforms and mutants with low nanomolar IC_{50} values; directly blocks cell growth and indirectly inhibits angiogenesis

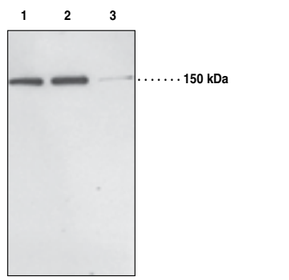
25 mg
50 mg
100 mg
250 mg



PH Domain Leucine-rich Repeat Protein Phosphatase 1 Polyclonal Antibody 10007191

KIAA0606 Protein, PHLPP1, PLEKHE1 Protein, SCOP, Suprachiasmatic Nucleus Circadian Oscillatory Protein
Peptide affinity-purified IgG **Stability:** ≥1 year at 4°C
Summary: Antigen: human PHLPP1 amino acids 1192-1205 of the α isoform, or amino acids 1704-1717 of the β isoform • Host: rabbit • Cross Reactivity: (+) human, mouse, rat PHLPP1α and PHLPP1β, (-) PHLPP2 • Application(s): ICC, IHC (paraffin-embedded sections), and WB • PHLPP1 and PHLPP2 dephosphorylate the hydrophobic motif of Akt and thus reduce Akt activity, resulting in an increase in the number of apoptotic cells.

500 µl



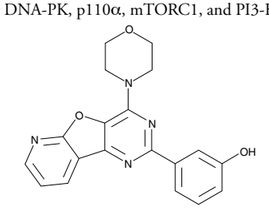
Lane 1: Mouse brain homogenate (40 µg)
Lane 2: Mouse brain homogenate (60 µg)
Lane 3: Human hippocampus supernatant (60 µg)

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

PI-103 10009209

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

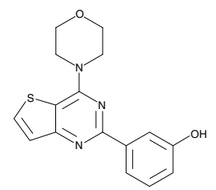
1 mg
5 mg
10 mg
25 mg



PI3-Kinase α Inhibitor 2 10010177

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

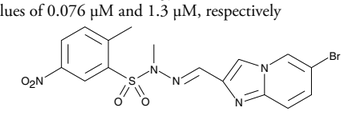
500 µg
1 mg
5 mg
10 mg



PIK-75 10009210

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

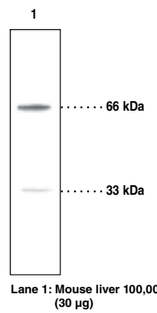
1 mg
5 mg
10 mg
25 mg



PINK1 Polyclonal Antibody 10006283

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

500 µl
Trial Size



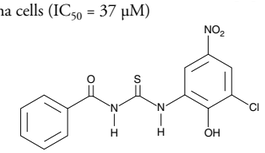
Lane 1: Mouse liver 100,000 x g pellet (30 µg)

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

PIT-1 10728

[53501-41-0]
MF: $C_{14}H_{10}ClN_3O_4S$ **FW:** 351.8 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A selective nonphosphoinositide inhibitor that specifically disrupts PIP_3/Akt PH domain binding (IC_{50} = 31 µM); suppresses PI3K-PDK1-Akt-dependent phosphorylation, which reduces cell viability and induces apoptosis in PTEN-deficient U87MG glioblastoma cells (IC_{50} = 37 µM)

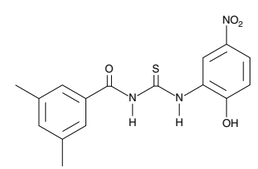
5 mg
10 mg
50 mg
100 mg



3,5-dimethyl PIT-1 10727

[701947-53-7]
MF: $C_{16}H_{15}N_3O_4S$ **FW:** 345.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A selective nonphosphoinositide inhibitor with favorable solubility *in vivo* that specifically disrupts PIP_3/Akt PH domain binding (IC_{50} = 27 µM); suppresses PI3K-PDK1-Akt-dependent phosphorylation, which reduces cell viability and induces apoptosis in PTEN-deficient U87MG glioblastoma cells (IC_{50} = 36 µM)

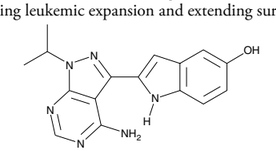
1 mg
5 mg
10 mg
25 mg



PP242 13643

[1092351-67-1]
MF: $C_{16}H_{16}N_6O$ **FW:** 308.3 **Purity:** ≥95%
A crystalline solid **Stability:** ≥1 year at -20°C
Summary: An inhibitor of the active site of mTOR kinase in both mTORC1 and mTORC2 (IC_{50} = 8 nM); shown to cause the death of leukemia cells more potently than rapamycin and, *in vivo*, delays leukemia onset and augments the effects of tyrosine kinase inhibitors in suppressing leukemic expansion and extending survival

1 mg
5 mg
10 mg



PTEN (human recombinant) 10009746

MMAC1, Phosphatase and Tensin Homology on Chromosome, Phosphatidylinositol 3-phosphatase, TEP1
M_r: 50.8 kDa **Purity:** ≥95%
Source: Recombinant N-terminal His-tagged protein purified from *Sf*21 cells

25 µg
50 µg
100 µg

•Also Available: **PTEN Western Ready Control** (10009747)

PTEN Polyclonal Antibody 10005059

MMAC1, Phosphatase and Tensin Homolog on Chromosome 10, Phosphoinositide 3-phosphatase, TEP1

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

Antigen: human PTEN amino acids 254-270 • **Host:** rabbit • Cross Reactivity: (+) human, mouse, and rat PTEN • Application(s): IHC (paraffin-embedded sections) and WB • PTEN dephosphorylates proteins and lipids such as Akt and PIP_3 and therefore functions as a key regulatory enzyme in a central signal transduction pathway. PTEN is considered a tumor suppressor as loss-of-function mutations in PTEN often result in human cancers including melanoma and prostate carcinoma.

500 µl

•Also Available: **PTEN Blocking Peptide** (10007073)
PTEN Western Ready Control (10009747)

SC-66 10876

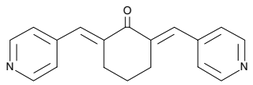
[871361-88-5]

MF: $C_{18}H_{16}N_2O$ **FW:** 276.3 **Purity:** ≥98%

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

Summary: An allosteric inhibitor of Akt that facilitates both ubiquitination and deactivation of Akt; inhibits Akt activity in HEK293T cells, promoting cell death; suppresses tumor growth in mice

5 mg
10 mg
25 mg
100 mg



TGX-221 10007349

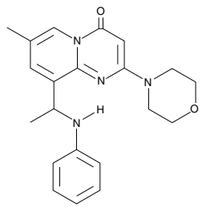
[663619-89-4]

MF: $C_{21}H_{24}N_4O_2$ **FW:** 364.4 **Purity:** ≥98%

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

Summary: A potent, selective, and cell permeable inhibitor of PI3K p110β; IC_{50} increases from 5 to ~50 nM at ATP concentrations of 50 µM and 1 mM, respectively; inhibits PtdIns-(3,4)-P_2 production in platelets with an IC_{50} value of 50 nM

100 µg
500 µg
1 mg
5 mg



Triciribine 10010237

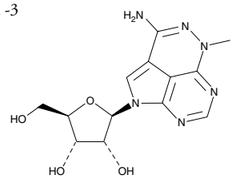
[35943-35-2] API 2, NSC 154020, Tricyclic Nucleoside

MF: $C_{13}H_{16}N_6O_4$ **FW:** 320.3 **Purity:** ≥98%

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

Summary: A cell-permeable tricyclic nucleoside that inhibits the phosphorylation, activation, and signaling of Akt-1, -2, and -3

1 mg
5 mg
10 mg



Wortmannin 10010591

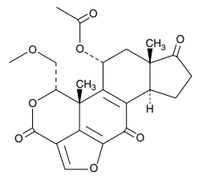
[19545-26-7] KY 12420

MF: $C_{23}H_{24}O_8$ **FW:** 428.4 **Purity:** ≥98%

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

Summary: A potent, cell-permeable, and irreversible inhibitor of PI3K enzymes (IC_{50} = 1-10 nM)

1 mg
5 mg
10 mg
25 mg



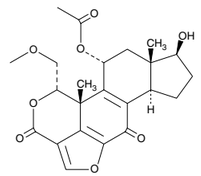
17β-hydroxy Wortmannin 13812

MF: $C_{23}H_{26}O_8$ **FW:** 430.4 **Purity:** ≥98%

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

Summary: An analog of wortmannin; irreversibly binds PI3K; inhibits recombinant PI3K and mTOR (IC_{50} = 2.7 and 193 nM, respectively) and prevents the growth of LNCap cells (IC_{50} = 1.46 µM)

500 µg
1 mg
5 mg
10 mg



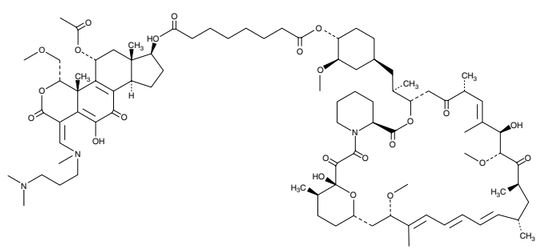
Wortmannin-Rapamycin Conjugate 13671

MF: $C_{88}H_{131}N_3O_{23}$ **FW:** 1,598.9 **Purity:** ≥98%

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

Summary: Consists of analog of 17-hydroxy wortmannin and rapamycin conjugated *via* a prodrug linker, which are released upon hydrolysis of the prodrug linker *in vivo*; inhibits the growth of tumors in mice better than rapamycin alone

500 µg
1 mg
5 mg
10 mg



PI3K/Akt Pathway Inhibitors

Item No.	Item Name	Target	Inhibitory Concentration
13622	**AS 041164**	PI3Kγ	IC_{50} = 70 nM
10009052	**AS 252424**	PI3Kγ	IC_{50} = 30 nM
10010175	**AS 604850**	PI3Kγ	IC_{50} = 0.25 µM
10007707	**AS 605240**	PI3Kγ	IC_{50} - 8 nM
10009078	**CAY10505**	PI3Kγ	IC_{50} = 30 nM
10010233	**CAY10567**	Akt1	IC_{50} = ~ 12.5 µM
13838	**CAY10626**	PI3Kα mTOR	IC_{50} = 0.9 nM IC_{50} = 0.6 nM
70920	**LY294002**	PI3K	IC_{50} = 1.4 µM
10010236	**ML-9**	PKB/Akt	IC_{50}= 10-50 µM in rat primary adipocytes
10565	**NVP-BEZ235**	PI3K/mTOR	Inhibits PI3K isoforms and mutants with low nanomolar IC_{50} values
10009209	**PI-103**	DNA-PK p110α mTORC1 PI3-KC2β p110δ mTORC2 p110β p110γ	IC_{50} = 2 nM IC_{50} = 8 nM IC_{50} = 20 nM IC_{50} = 26 nM IC_{50} = 48 nM IC_{50} = 83 nM IC_{50} = 88 nM IC_{50} = 150 nM
10010177	**PI3-Kinase α Inhibitor 2**	PI3Kα	IC_{50} = 2 nM
10009210	**PIK-75**	p110α	IC_{50} = 5.8 nM
10728	**PIT-1**	Inhibits PIP_3/Akt PH domain binding	IC_{50} = 31 µM
10727	**3,5-dimethyl PIT-1**	Inhibits PIP_3/Akt PH domain binding	IC_{50} = 27 µM
13643	**PP242**	Active site of mTORC1 and mTORC2	IC_{50} = 8 nM
13067	**SB 203580** Also Available: SB 203580 (hydrochloride) (13344)	PDK-1	IC_{50} = 3-5 µM
10010246	**SB 216763**	GSK3α	IC_{50} = 34 nM
10876	**SC-66**	Akt	
10007349	**TGX-221**	p110β	IC_{50} = 50 nM in platelets
10010237	**Triciribine**	Akt	IC_{50} = ~ 5-10 µM in Akt-overexpressing human cancer cell lines
10010591	**Wortmannin** Also Available: Wortmannin-Rapamycin Conjugate (13671)	PI3K	IC_{50} = 1-10 nM
13812	**17β-hydroxy Wortmannin**	PI3K mTOR	IC_{50} = 2.7 IC_{50} = 193 nM

Thomas G. Brock, Ph.D.

Receptors and Tyrosine Kinases

Central to cell signaling are two types of proteins, the receptors and the kinases. The former perceive and respond to the extracellular cues that arrive at a cell's surface, while the latter propagate the response within the cell by phosphorylation and altering the activity of assorted specific targets. The receptor tyrosine kinases (RTK) integrate these functions, responding to extracellular cues by phosphorylating intracellular targets. Closely related are a group of receptors which, before or after activation, bind TKs to initiate signaling. Many RTKs and receptor-associated TKs direct events essential to cell division, cellular differentiation, and morphogenesis. As a result, their actions are central to ontogeny and development, as well as diseases like cancer. This article gives a brief overview of RTKs.

The Human Tyrosine Kinases

The human kinome was characterized almost a decade ago.[1] Human TKs are a large family with some 90 members which can be organized phylogenetically (Figure 1). Functionally, the TKs can be separated into RTKs and non-receptor TKs (also called cytoplasmic TKs, CTK). RTK, but not CTK, have a transmembrane helix separating the kinase domain from a ligand binding domain. Interestingly, the RTKs, shown in blue in Figure 1, are not neatly segregated from CTKs (in red) when organized phylogenetically. As a group, the TKs are newer than their functional analogs, the Ser/Thr kinases. The TKs are absent from plants and unicellular organisms like *Dictyostelium* and yeast. Moreover, certain families have shown substantial expansion in humans: there are 14 genes for the Eph family RTKs in humans but only 1 in flies. Such expansion is thought to relate to a role for these RTKs in processes that are more advanced in humans, such as angiogenesis, hematopoiesis, and functioning of the nervous and immune systems.[1]

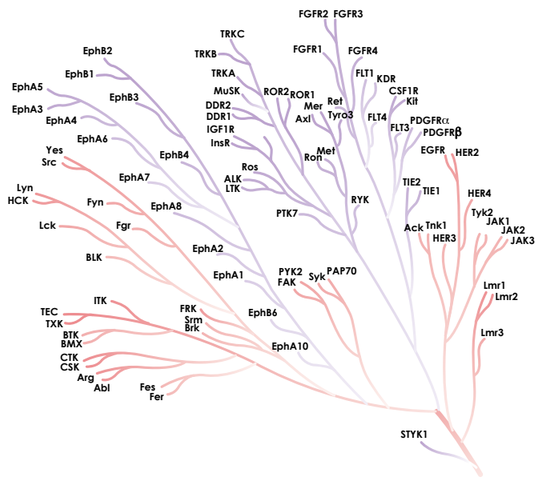


Figure 1. Phylogenetic relationships of the human tyrosine kinases (receptor tyrosine kinases: blue; non-receptor tyrosine kinases: red); modified from www.kinase.com/human/kinome

Diversity in Structure and Substrate

The 50-plus human RTKs have been divided into some 20 families.[2] As the Eph family has 14 members, the remaining families are very small. The splintering of the RTKs into numerous families reflects diversity of structure, which in turn relates to the variety of agonists which act specifically at each type of receptor. An examination of individual members of each of the branches of the TK tree reveals certain notable findings (Figure 2). First, many of the CTKs contain either Src homology 2 (SH2) or SH3 domains, or both. These domains are involved in binding the TK to other proteins. The SH2 domain specifically recognizes phosphorylated tyrosine residues. Thus, a CTK may bind an activated (and autophosphorylated) RTK *via* an SH2 domain, only to then tyrosine phosphorylate its own substrate. Other CTKs contain additional domains which move the kinase to specific positions within the cell and in this way control the subcellular targeting of kinase activity. For example, JAKs contain a FERM domain, which positions these CTKs on cytoplasmic tails of receptors for cytokines and polypeptide hormones.[3] Another point of interest centers on the kinase domains. While most TKs have highly similar kinase domains, many growth factor RTKs (*e.g.*, FGF receptors) have large inserts in the conserved sequence. Similarly, the TRKC kinase domain is 20% larger than the classic domain because of numerous small inserts. The JAKs contain 2 kinase-like domains, with the C-terminal one displaying activity and the other serving a regulatory role. Finally, the RTKs have many types of ligand binding domains (LBD), hinting at the diversity of potential ligands. Remarkably, even similarities in LBDs are misleading. For example, the ephrin LBDs of the EphA receptors generally bind a different class of ligand from those of the EphB RTKs. Similarly, both CSF1R and PDGFRα have clusters of five immunoglobulin-like domains for binding ligands, yet they have distinct agonists. The apparent absence of LBDs on HER2 (EGFR2) invites further consideration of the related receptor, EGFR.

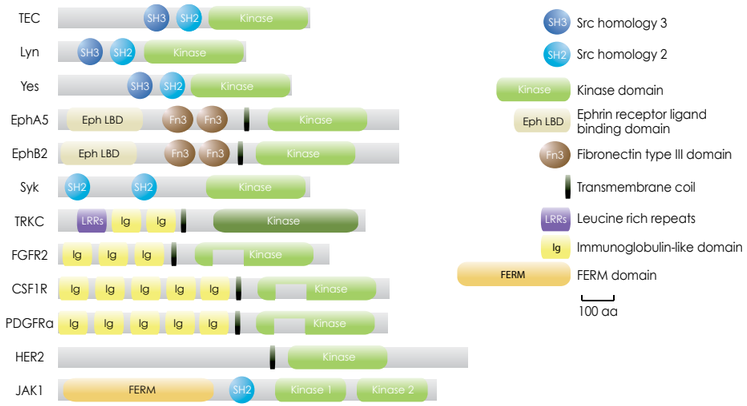


Figure 2. Structural features of representative TKs from different branches of the TK phylogenetic tree

EGFR Signaling

EGFR, also known as HER1 or erbB1, is one of four related RTKs which can homo- or heterodimerize following ligand binding. EGFR binds EGF, TGF-α, amphiregulin, or epigen and, after dimerization, undergoes autophosphorylation (Figure 3). These tyrosine phosphorylated sites are targeted by the SH2 domains on a variety of proteins, including Grb2, Shc1, p85α and β, PLCγ, and JAK1.[4] Grb2 and Shc1, with SOS, signal to activate the Ras/Raf/MEK/ERK1,2 pathway, altering gene expression and promoting cell proliferation. Through p85α and β, PI3K converts phosphatidylinositol (4,5)-bisphosphate (PIP_2) to phosphatidylinositol (3,4,5)-trisphosphate (PIP_3) and directs PKD1 to activate Akt, which promotes cell survival through several mechanisms (see related story on page 4). PLCγ mediates hydrolysis of PIP_2 to give inositol (1,4,5)-trisphosphate (IP_3) and DAG, leading to the release of calcium from intracellular stores and the activation of certain PKC isoforms, which can alter gene expression, cell mobility, and, in cancer, metastasis. JAK1, through STAT3, alters gene expression related to cell survival and proliferation.

There are four genes encoding EGFR family products, with the four full length products named HER1-4 (erbB1-4). Importantly, the different monomers can homo- or heterodimerize, with profound implications. As noted earlier, HER2 has no recognized LBD, but it can dimerize with EGFR (HER1) and signal in response to ligands that activate EGFR. Or, HER2 can dimerize with HER3 and facilitate its signaling through its ligands, the neuregulins. HER3 itself has a neuregulin binding domain but lacks an active kinase domain, and thus requires heterodimerization for signaling. Amplification or overexpression of either HER2 or HER3 occurs in numerous cancers. HER4 is also activated by neuregulins. Alternatively-spliced transcriptional variants as well as proteolytic cleavage products of these receptors act outside the cell or within the nucleus to evoke a wide range of effects.

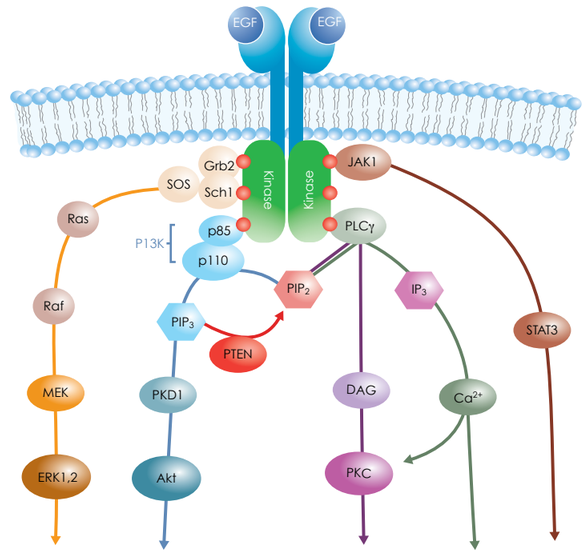


Figure 3. Signaling through EGFR

Signaling initiated by interferon-γ (IFN-γ)

IFN-γ is a cytokine with prominent anti-viral, immunoregulatory, and anti-tumor roles and is a potent activator of macrophages. Produced primarily by activated T-cells, natural killer (NK), and NKT-cells, IFN-γ acts as a dimer when binding to its multimeric receptor, IFNGR (Figure 4). The IFNGR receptor consists of two α subunits (IFNGR1), which combine to form an LBD and have long cytoplasmic tails, and two β subunits (IFNGR2), which lack an LBD and have relatively short cytoplasmic tails.[5,6] Each subunit has an inactive form of JAK constitutively bound to its intracellular domain, with JAK1 on α subunits and JAK2 on β subunits. The initial interaction of a single IFN-γ dimer with the LBD of an α subunit triggers receptor assembly followed by JAK1-JAK2 transactivation. Tyrosine phosphorylation of the tails of both α subunits by JAKs provides docking sites for two Stat1 molecules, which are then phosphorylated by JAKs. This releases the Stat1 pair, which dimerize and translocate to the nucleus to alter gene expression.

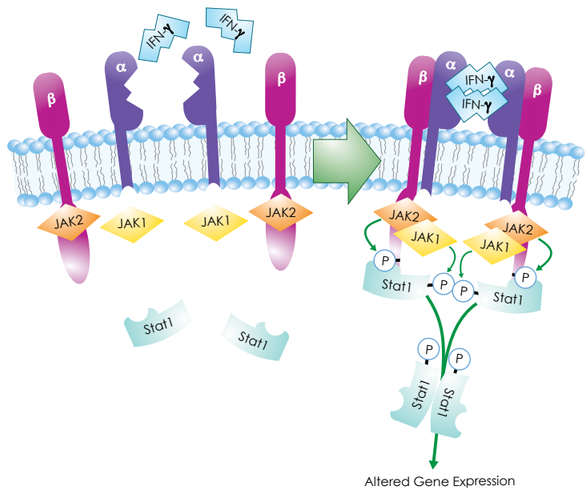


Figure 4. IFN-γ signals through IFNGR to activate JAK/STAT signaling

Future Directions

A large selection of TK inhibitors have been developed for research applications and are available from Cayman Chemical (please see Table on page 18). Inhibitors of both RTKs and CTKs are also headlining the pharmaceutical news. For example, currently available multi-targeted VEGF tyrosine kinase inhibitors (TKI) have been approved for treating renal cell carcinoma. These TKI, which include sunitinib, sorafenib, and pazopanib, are effective but have off-target effects. An oral inhibitor of SYK, PRT062607, shows potential for the treatment of rheumatoid arthritis as well as other autoimmune and inflammatory diseases. These examples suggest the importance of TKs in pathogenesis.

References

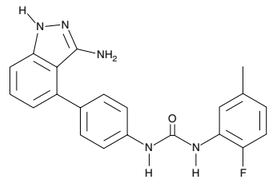
1. Manning, G., Whyte, D.B., Martinez, R., *et al.* Science **298,** 1912-1934 (2002).
2. Robinson, D.R., Wu, Y.-M., and Lin, S.-F. Oncogene **19,** 5548-5557 (2000).
3. Yamaoka, K., Saharinen, P., Pesu, M., *et al.* Genome Biol. **5(12),** 1-6 (2004).
4. Ono, M. and Kuwano, M. Clin. Cancer Res. **12,** 7242-7251 (2006).
5. Kotenko, S.V., Izotova, L.S., Pollack, B.P., *et al.* J. Biol. Chem. **270(36),** 20915-20921 (1995).
6. Bach, E.A., Tanner, J.W., Marsters, S., *et al.* Mol. Cell. Biol. **16(6),** 3214-3221 (1996).

Tyrosine Kinase Signaling

ABT-869 13653

[796967-16-3] Linifanib
MF: $C_{21}H_{18}FN_5O$ **FW:** 375.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥1 year at -20°C
Summary: An ATP-competitive, multi-targeted RTK inhibitor that inhibits all members of the VEGF and PDGFRfamilies (IC_{50}s = 4-190 nM); inhibits proliferation of MV-4-11 and MOLM-13 cells (IC_{50}s = 4 and 6 nM, respectively)

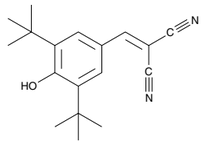
1 mg
5 mg
10 mg
50 mg



AG-17 10010248

[10537-47-0] GCP 5126, Malonoben, NSC 242557, RG-50872, SF 6847, Tyrphostin 9, Tyrphostin AG-17
MF: $C_{18}H_{22}N_2O$ **FW:** 282.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An inhibitor of EGFR kinase with an IC_{50} value of 460 µM in the human epidermoid carcinoma cell line A431

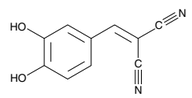
5 mg
10 mg
25 mg
50 mg



AG-18 10010300

[118409-57-7] RG-50810, RG-50858, TX 825, Tyrphostin 23, Tyrphostin AG-18
MF: $C_{10}H_6N_2O_2$ **FW:** 186.1 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An inhibitor of EGFR kinase with an IC_{50} value of 35 µM in the human epidermoid carcinoma cell line A431

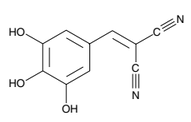
5 mg
10 mg
25 mg
50 mg



AG-82 10010312

[118409-58-8] NSC 676484, RG-50875, Tyrophostin 25, Tyrphostin AG-82
MF: $C_{10}H_6N_2O_3$ **FW:** 202.2 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An inhibitor of EGFR kinase with an IC_{50} value of 3 µM in the human epidermoid carcinoma cell line A431

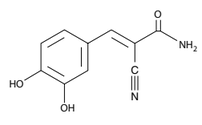
5 mg
10 mg
25 mg
50 mg



AG-99 10010313

[122520-85-8] Tyrphostin 46
MF: $C_{10}H_8N_2O_3$ **FW:** 204.2 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An inhibitor of EGFR kinase with an IC_{50} value of 10 µM in the human epidermoid carcinoma cell line A431

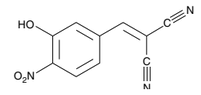
5 mg
10 mg
25 mg
50 mg



AG-126 13297

[1118409-62-4] 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

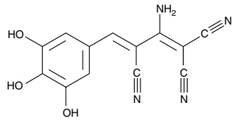
1 mg
5 mg
10 mg
25 mg



AG-183 10010315

[122520-90-5] Tyrphostin 51
MF: $C_{13}H_8N_4O_3$ **FW:** 268.2 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An inhibitor of EGFR kinase with an IC_{50} value of 0.8 µM in the human epidermoid carcinoma cell line A431

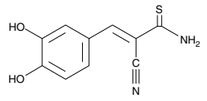
5 mg
10 mg
25mg
50 mg



AG-213 10010314

[122520-86-9] Tyrphostin 47, Tyrphostin AG-213
MF: $C_{10}H_8N_2O_2S$ **FW:** 220.2 **Purity:** ≥97%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An inhibitor of EGFR kinase with an IC_{50} value of 2.4 µM in the human epidermoid carcinoma cell line A431

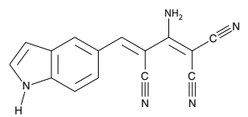
5 mg
10 mg
25 mg
50 mg



AG-370 10010568

[134036-53-6] NSC 651712
MF: $C_{15}H_9N_5$ **FW:** 259.3 **Purity:** ≥95% (*cis/trans* mixture)
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A selective inhibitor of PDGFRkinase with an IC_{50} value of 20 µM in human bone marrow; inhibits the EGF receptor with an IC_{50} value of 820 µM

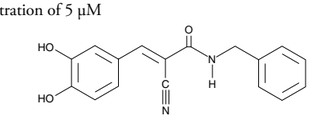
1 mg
5 mg
10 mg
25 mg



AG-490 10010311

[133550-30-8]
MF: $C_{17}H_{14}N_2O_3$ **FW:** 294.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An selective inhibitor of JAK2 activity that blocks leukemic cell growth *in vitro* and *in vivo* by inducing programmed cell death; blocks growth of all pre-B acute leukemia (ALL) cells at a concentration of 5 µM

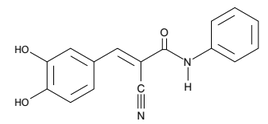
5 mg
10 mg
25 mg
50 mg



AG-494 10010242

[133550-35-3]
MF: $C_{16}H_{12}N_2O_3$ **FW:** 280.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An inhibitor of EGFR kinase with an IC_{50} value of 1 µM in HT-22 cells

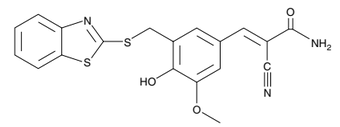
5 mg
10 mg
25 mg
50 mg



AG-825 10010243

[149092-50-2] Tyrphostin AG-825
MF: $C_{19}H_{15}N_3O_3S_2$ **FW:** 397.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A selective ATP-competitive inhibitor of the tyrosine kinase activity of HER-2/*neu* (IC_{50} = 0.35 µM)

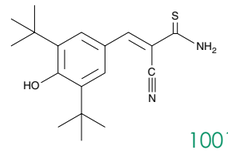
1 mg
5 mg
10 mg
50 mg



AG-879 10793

[148741-30-4] Tyrphostin AG-879
MF: $C_{18}H_{24}N_2O_6$ **FW:** 316.5 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A tyrphostin compound that inhibits nerve growth factor (NGF)-dependent TrkA tyrosine phosphorylation in PC-12 cells (IC_{50} ~40µM), HER2-ErbB2 kinase in several breast and ovarian cancer cell lines (IC_{50} ~0.5 µM), and the VEGF receptor FLK-1 (IC_{50} ~1 µM)

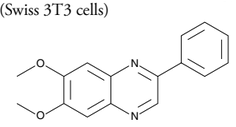
5 mg
10 mg
25 mg
50 mg



AG-1296 10010592

[146535-11-7] Tyrphostin AG-1296
MF: $C_{16}H_{14}N_2O_2$ **FW:** 266.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent and selective inhibitor of PDGFRkinase with an IC_{50} value of about 0.4 µM both *in vitro* and in cells (Swiss 3T3 cells)

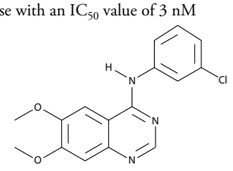
1 mg
5 mg
10 mg
25 mg



AG-1478 10010244

[153436-53-4] NSC 693255, Tyrphostin AG-1478
MF: $C_{16}H_{14}ClN_3O_2$ **FW:** 315.8 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An inhibitor of EGFR kinase with an IC_{50} value of 3 nM

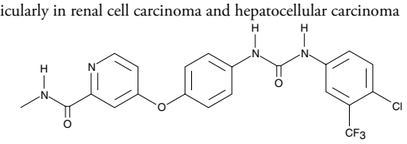
1 mg
5 mg
10 mg
25 mg



BAY-43-9006 10009644

[284461-73-0] Nexovar®, Sorafenib
MF: $C_{21}H_{16}ClF_3N_4O_3$ **FW:** 464.8 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An inhibitor of Raf-1 and B-Raf (IC_{50} = 6 and 22 nM, respectively), as well as several RTKs, including VEGFR- 2 and -3, PDGFR-β, Flt-3, and c-KIT (IC_{50} = 90, 15, 20, 57, and 58 nM); inhibits tumor angiogenesis and induces tumor cell apoptosis, particularly in renal cell carcinoma and hepatocellular carcinoma

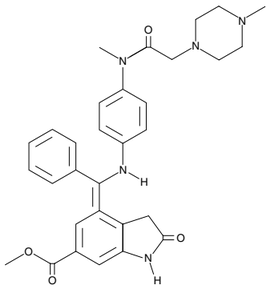
1 mg
5 mg
10 mg
50 mg



BIBF 1120 11022

[928326-83-4] Vargatef™
MF: $C_{31}H_{33}N_5O_4$ **FW:** 539.6 **Purity:** ≥95%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A triple RTK inhibitor, blocking signaling through VEGFR (IC_{50} values of 13 to 34 nM), PDGFR (IC_{50} values of 59 to 65 nM), and FGFR (IC_{50} values of 37 to 610 nM); inhibits angiogenesis; has potential applications in various forms of cancer and pulmonary fibrosis

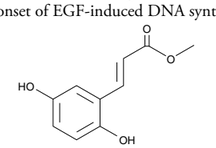
5 mg
10 mg
50 mg
100 mg



Erbstatin Analog 10010238

[63177-57-1] Methyl 2,5-dihydoxycinnamate
MF: $C_{10}H_{10}O_4$ **FW:** 194.2 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A stable, potent analog of erbstatin; inhibits EGFR tyrosine kinase *in vitro* with an IC_{50} of 0.14 µg/ml; inhibits EGF-stimulated growth in NIH3T3 cells with an IC_{50} value of 0.5 µg/ml; delays onset of EGF-induced DNA synthesis

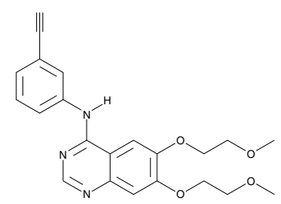
1 mg
5 mg
10 mg
50 mg



Erlotinib 10483

[183321-74-6] CP 358,774, NSC 718781, Tarceva™
MF: $C_{22}H_{23}N_3O_4$ **FW:** 393.2 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A tyrosine kinase inhibitor which acts on EGFR, inhibiting EGFR-associated kinase activity (IC_{50} = 2.5 µM) and tumor growth in human HN5 tumor xenografts in mice with an ED_{50} value of 9 mg/kg; drug form of Erlotinib, Tarceva™, is used to treat certain forms of cancer

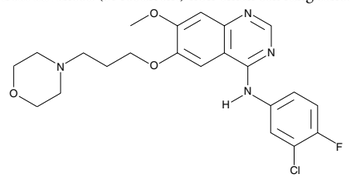
250 mg
500 mg
1 g
5 g



Gefitinib 13166

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

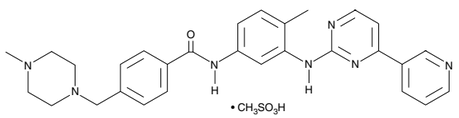
250 mg
500 mg
1 g
5 g



Imatinib (mesylate) 13139

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

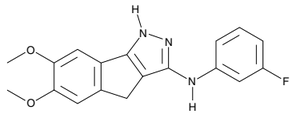
25 mg
50 mg
100 mg
500 mg



JNJ-10198409 10008131

[627512-69-0]
MF: $C_{18}H_{16}FN_3O_2$ **FW:** 325.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An inhibitor of PDGF-BB tyrosine kinase with an IC_{50} value of 4.2 nM when tested in human coronary artery smooth muscle cells

1 mg
5 mg
10 mg
50 mg



Kinase Screening Library (96-Well) 10505

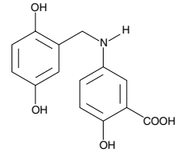
A 10 mM solution in DMSO **Stability:** ≥2 years at -20°C
Summary: This screening plate includes various kinase inhibitors

100 µl

Lavendustin C 10010329

[125697-93-0] HDBA, NSC 666251
MF: $C_{14}H_{13}NO_5$ **FW:** 275.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent inhibitor of EGFR-associated tyrosine kinase with an IC_{50} value of 0.012 µM that also inhibits pp60c-src(+) kinase and CamKII with IC_{50} values of 0.5 and 0.2 µM, respectively

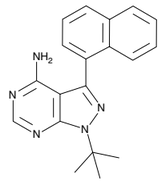
1 mg
5 mg
10 mg
50 mg



1-NA-PP1 10954

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

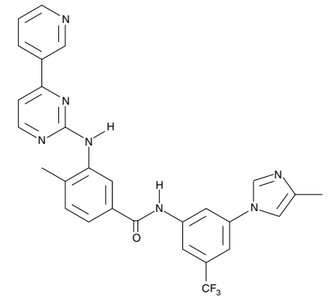
1 mg
5 mg
10 mg
50 mg



Nilotinib 10010422

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

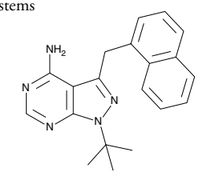
5 mg
10 mg
25 mg
50 mg



1-NM-PP1 13330

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

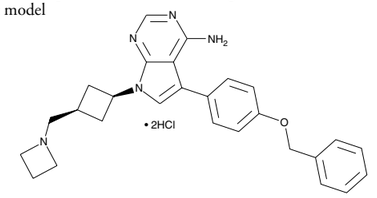
1 mg
5 mg
10 mg
25 mg



NVP-AEW541 (hydrochloride) 13641

MF: $C_{27}H_{29}N_5O \bullet 2HCl$ **FW:** 512.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A selective IGF-1R kinase inhibitor (IC_{50} = 0.086 µM); prevents IGF-I-mediated survival and proliferation of MCF-7 cells (IC_{50} = 0.16 and 1.64 µM, respectively); dose-dependently inhibits tumor growth in a mouse NWT-21 fibrosarcoma tumor model

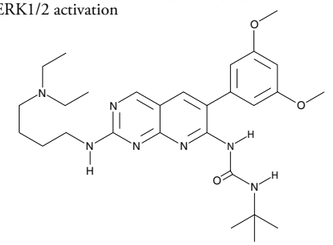
500 µg
1 mg
5 mg
10 mg



PD 173074 13032

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

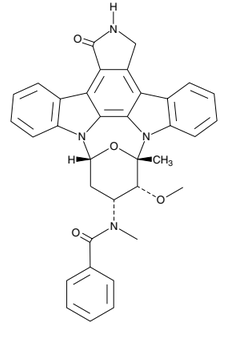
1 mg
5 mg
10 mg
25 mg



PKC 412 10459

[120685-11-2] N-Benzoylstaurosporine, CGP 41231, CGP 41251, Midostaurin
MF: $C_{35}H_{30}N_4O_4$ **FW:** 570.6 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A cell-permeable, reversible inhibitor of several kinases, including PKCα, PKCβ, PKCγ, Syk, Flk-1, Akt, PKA, c-Kit, C-Fgr, c-Src, FLT3, PDFRβ, VEGFR1, and VEGFR2, with IC_{50} values ranging from 80-500 nM

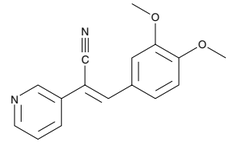
1 mg
5 mg
10 mg
50 mg



RG-13022 10010309

[149286-90-8]
MF: $C_{16}H_{14}N_2O_2$ **FW:** 266.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An inhibitor of EGFR kinase with an IC_{50} value of 1 µM in HT-22 cells

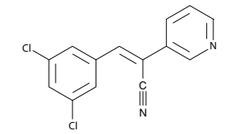
5 mg
10 mg
50 mg
100 mg



RG-14620 10010310

[136831-49-7]
MF: $C_{14}H_8Cl_2N_2$ **FW:** 275.1 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An inhibitor of EGFR kinase with an IC_{50} value of 3 µM in HT-22 cells

5 mg
10 mg
50 mg
100 mg



Receptor Tyrosine Kinase Inhibitors

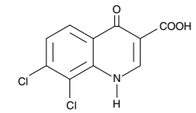
Item No.	Item Name	Target	Effective Concentration
13653	**ABT-869**	VEGFR PDGFR	IC_{50} = range from 4-190 nM
10010248	**AG-17**	EGFR kinase	IC_{50} = 460 µM in human epidermoid carcinoma A431 cells
10010300	**AG-18**	EGFR kinase	IC_{50} = 35 µM in human epidermoid carcinoma A431 cells
10010312	**AG-82**	EGFR kinase	IC_{50} = 3 µM in human epidermoid carcinoma A431 cells
10010313	**AG-99**	EGFR kinase	IC_{50} = 10 µM in human epidermoid carcinoma A431 cells
13297	**AG-126**	EGFRK PDGFRK	IC_{50} = 450 µM IC_{50} > 100 µM
10010315	**AG-183**	EGFR kinase	IC_{50} = 0.8 µM in human epidermoid carcinoma A431 cells
10010314	**AG-213**	EGFR kinase	IC_{50} = 2.4 µM in human epidermoid carcinoma A431 cells
10010568	**AG-370**	PDGFR kinase EGFR	IC_{50} = 20 µM in human bone marrow fibroblasts IC_{50} = 820 µM
10010242	**AG-494**	EGFR kinase	IC_{50} = 1 µM in HT- 22 cells
10010243	**AG-825**	Her-2/neu EGFR PDGFR	IC_{50} = 0.35 µM IC_{50} = 19 µM IC_{50} = 40 µM
10793	**AG-879**	NGF-dependent TrKA Tyrosine-phosphorylation HER2/ErbB2 kinase VEGF receptor FLK-1	 IC_{50} ~ 40 µM IC_{50} ~ 0.5 µM IC_{50} ~ 1µM
10010592	**AG-1296**	PDGFR kinase	IC_{50} = 0.4 µM (both *in vitro* and in Swiss 3T3 cells)
10010244	**AG-1478**	EGFR kinase	IC_{50} = 3 nM
10009644	**BAY-43-9006**	VEGFR-2 VEGFR-3 PD GFR-β FH-3 c-Kit	IC_{50} = 90 nM IC_{50} = 15 nM IC_{50} = 20 nM IC_{50} = 57 nM IC_{50} = 58 nM
11022	**BIB F 1120**	VEGFR PDGFR FGFR	IC_{50} = 13-34 nM IC_{50} = 59-65 nM IC_{50} = 37-610 µM
10010238	**Erbstatin Analog**	EGFR kinase	IC_{50} = 0.14 µg/ml
10483	**Erlotinib**	EGFR	IC_{50} = 2.5 µM (mouse recombinant) and 10 µM (*Xenopus*)
13166	**Gefitinib**	EGFR kinase	IC_{50} = 0.2-0.4 µM in various cancer cell lines
10010329	**HDBA**	EGFR kinase	IC_{50} = 0.012 µM
13139	**Imatinib (mesylate)**	c-ABL PDGFR Kit BCPABL	
10008131	**JNJ-10198409**	PDGF-BB tyrosine kinase	IC_{50} = 4.2 nM
13341	**LY364947**	TGF-β R1	IC_{50} = 59 nM
13641	**NVP-AEW541 (hydrochloride)**	IGF-1R kinase	IC_{50} = 0.086 µM
13032	**PD 173074**	FGFR1 autophosphorylation	IC_{50} = 21.5 nM
10010309	**RG-13022**	EGFR kinase	IC_{50} = 1 µM in HT- 22 cells
10010310	**RG-14620**	EGFR kinase	IC_{50} = 3 µM in HT- 22 cells
13577	**SU 11652**	PDGFR VEGFR-2 FGFR1	IC_{50} = 3 nM IC_{50} = 27 nM IC_{50} = 170 nM

Ser/Thr Kinase Signaling

CAY10577 — 10011256

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

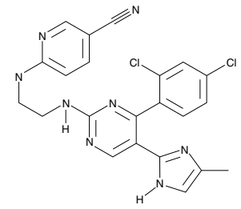
1 mg
5 mg
10 mg
50 mg



CHIR99021 — 13122

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

1 mg
5 mg
10 mg



GSK3β (Phospho-Ser^9) Polyclonal Antibody — 10009374

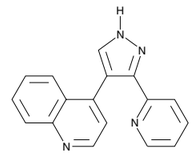
Anti-Phospho-Ser^9 Glycogen Synthase Kinase 3β
Peptide affinity-purified **Stability:** ≥1 year at -20°C
Summary: Antigen: phosphopeptide corresponding to amino acid residues surrounding the phospho-Ser9 of GSK3β • Host: rabbit • Cross Reactivity: (+) rat GSK3β • Application(s): WB • GSK3 is a Ser/Thr kinase that is involved in the regulation of many signaling pathways. GSK3β plays a key inhibitory role in both the insulin and Wnt signaling pathways.

1 ea

LY364947 — 13341

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

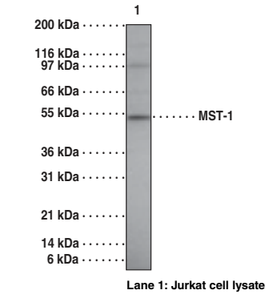
5 mg
10 mg
25 mg
50 mg



Mammalian STE-20-Like Kinase 1 Polyclonal Antibody — 13776

KRS2, MST-1, STK4
Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: synthetic peptide from human MST-1 amino acids 372-390 • Host: rabbit • Cross Reactivity: (+) human MST-1 • Application(s): WB • MST-1 is a Ser/Thr kinase that, upon cleavage, has been implicated in the promotion of chromatin condensation. The C-terminus of MST-1 contains two functional nuclear export signals, which are released upon caspase-mediated cleavage. The N-terminus portion of the protein then translocates to the nucleus and promotes chromatin condensation at sufficiently high levels. Full-length MST-1 is localized to the cytoplasm.

1 ea

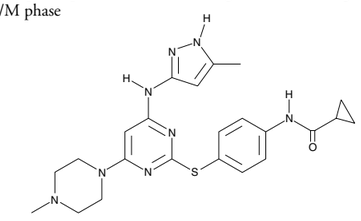


Lane 1: Jurkat cell lysate

MK 0457 — 13600

[639089-54-6] Tozasertib, VX 680
MF: $C_{23}H_{28}N_8OS$ **FW:** 464.6 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent pan-Aurora kinase inhibitor that favors Aurora A (K_i = 0.6 nM) over Aurora B (K_i = 18 nM) or Aurora C (K_i = 4.6 nM); inhibits proliferation of clear cell renal carcinoma (IC_{50} < 10 µM), inhibits histone H3 phosphorylation, and increases apoptosis; disrupts bipolar spindle formation during mitosis, arresting cell cycle progression at the G_2/M phase

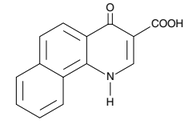
25 mg
50 mg
100 mg
250 mg



NSC 210902 — 10011255

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

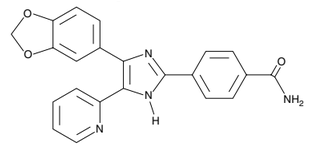
1 mg
5 mg
10 mg
50 mg



SB 431542 13031

[301836-41-9]
MF: $C_{22}H_{18}N_4O_3$ **FW:** 384.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent and selective inhibitor of the TGF-β1 receptor ALK5 (IC_{50} = 94 nM), ALK4 (IC_{50} = 140 nM) and, less effectively, ALK7; suppresses renewal in embryonic and induced pluripotent stem cells and promotes their differentiation

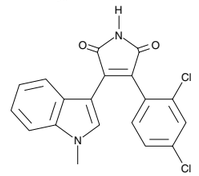
1 mg
5 mg
10 mg
25 mg



SB 216763 10010246

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

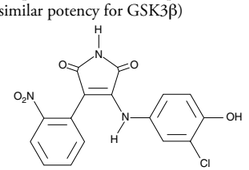
5 mg
10 mg
50 mg
100 mg



SB 415286 10010247

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

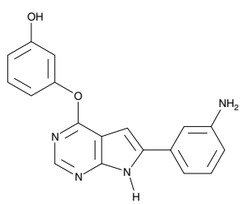
500 µg
1 mg
5 mg
10 mg



TWS119 10011251

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

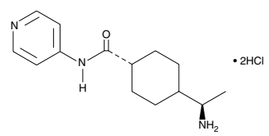
1 mg
5 mg
10 mg
25 mg



Y-27632 (hydrochloride) 10005583

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

500 µg
1 mg
5 mg
10 mg



SMAD Antibodies

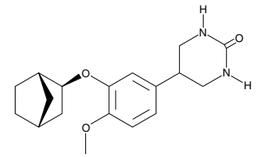
Item No.	Product Name
10822	SMAD1/5/8/9 Polyclonal Antibody
10821	SMAD1/5/8/9 Polyclonal Antiserm
10838	SMAD4 Polyclonal Antibody
10839	SMAD6 Polyclonal Antibody
10845	SMAD7 Polyclonal Antibody
10840	SMAD7 Polyclonal Antibody (azide free)

cAMP/cGMP Signaling

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 PDE4 (IC_{50} = 1.27 µM for PDE4 *versus* >100 µM for PDE1, PDE2, PDE3, and PDE5); inhibits eosinophil superoxide production (IC_{50} < 0.6 µM) and blocks LPS-induced TNFα release from monocytes (IC_{50} = 0.22 µM); significantly reduces antigen-induced airway inflammation in atopic guinea pigs, monkeys, and mice

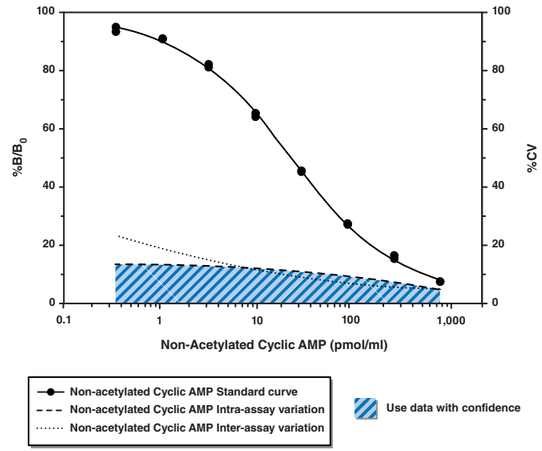
500 µg
1 mg
5 mg
10 mg



Cyclic AMP EIA Kit 581001

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

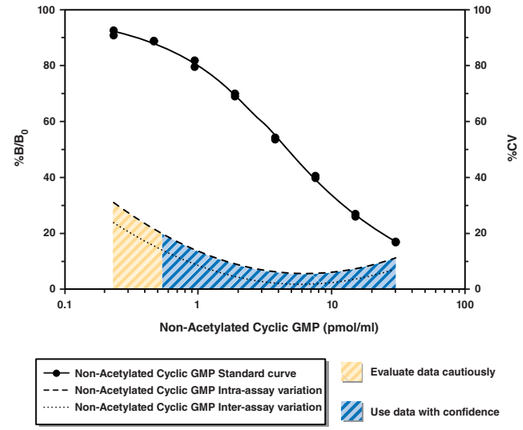
96 strip/solid wells
480 strip/solid wells



Cyclic GMP EIA Kit 581021

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

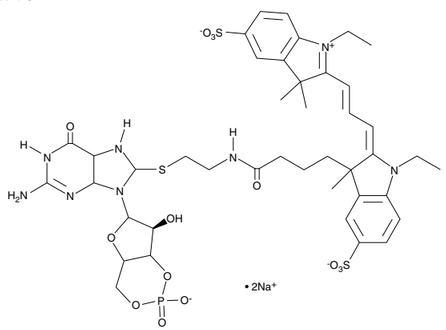
96 strip/solid wells
480 strip/solid wells



8-DY547-cGMP 10010109

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

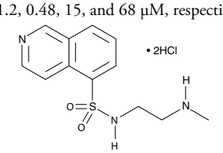
50 µg
100 µg



H-8 (hydrochloride) 10010249

[113276-94-1] Protein Kinase Inhibitor H-8
MF: $C_{12}H_{15}N_3O_2S$ • 2HCl **FW:** 338.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent inhibitor of PKA and PKG that shows moderate inhibition for PKC and MLCK with K_i values of 1.2, 0.48, 15, and 68 µM, respectively

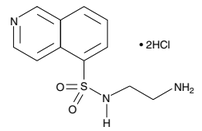
5 mg
10 mg
25 mg
50 mg



H-9 (hydrochloride) 13312

Protein Kinase Inhibitor H-9
MF: $C_{11}H_{13}N_3O_2S$ • 2HCl **FW:** 324.2 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent competitive inhibitor of PKC, PKG, and PKA with K_i values of 18, 0.87, and 1.9 µM, respectively

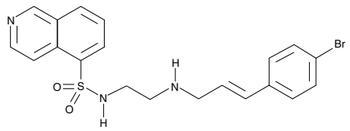
5 mg
10 mg
25 mg
50 mg



H-89 10010556

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

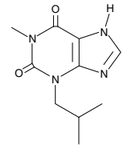
5 mg
10 mg
25 mg
50 mg



IBMX 13347

[28822-58-4] Isobutylmethylxanthine, 1-Methyl-3-Isobutylxanthine, NSC 165960
MF: $C_{10}H_{14}N_4O_2$ **FW:** 222.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A widely-used non-specific inhibitor of cAMP and cGMP PDEs (IC_{50} = 19, 50, 18, 13, 32, 7, and 50 µM for PDE1, PDE2, PDE3, PDE4, PDE5, PDE7, and PDE11, respectively)

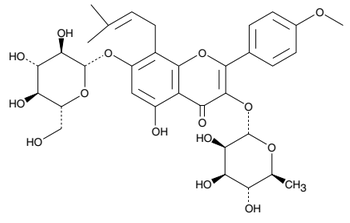
50 mg
100 mg
250 mg
500 mg



Icariin 13624

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

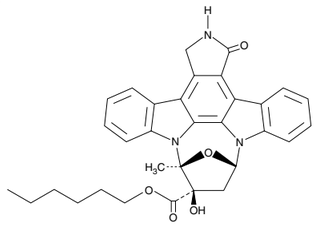
1 g
5 g
10 g
25 g



KT 5720 10011011

[108068-98-0]
MF: $C_{32}H_{31}N_3O_5$ **FW:** 537.6 **Purity:** ≥98%
A neat oil **Stability:** ≥1 year at -20°C
Summary: A potent inhibitor of PKA signaling that acts through competitive inhibition of ATP (K_i = 60 nM)

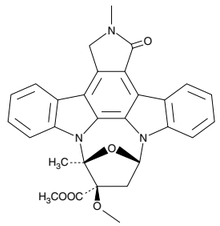
50 µg
100 µg
250 µg
500 µg



KT 5823 10010965

[126643-37-6]
MF: $C_{29}H_{25}N_3O_5$ **FW:** 495.5 **Purity:** ≥95%
A neat oil **Stability:** ≥1 year at -20°C
Summary: A potent, selective inhibitor of PKG (*in vitro* IC_{50} = 234 nM); cell-permeable and often used in intact cells to assess the role of PKG in signaling

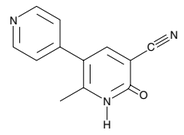
25 µg
50 µg
100 µg
250 µg



Milrinone 13357

[78415-72-2] Primacor®, WIN 47203
MF: $C_{12}H_9N_3O$ **FW:** 211.2 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent and selective inhibitor of type 3 PDEs, inhibiting recombinant PDE3A and PDE3B with IC_{50} values of 0.45 and 1.0 µM, respectively; has positive inotropic (stimulates cardiac muscle contractions) and vasodilatory effects when administered *in vivo*

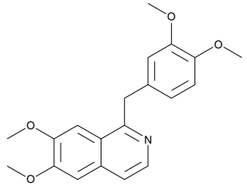
5 mg
10 mg
50 mg
100 mg



Papaverine 10011133

[58-74-2] NSC 136630
MF: $C_{20}H_{21}NO_4$ **FW:** 339.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An opium alkaloid that is structurally and pharmacologically distinct from opiates; inhibits PDE activity (IC_{50} = 13 µM) to increase cellular cAMP levels and alter cellular function; reduces heart and brain vasospasm and has been used to treat erectile dysfunction

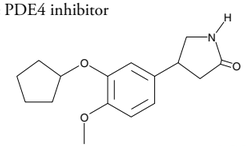
100 mg
250 mg
500 mg
1 g



Rolipram 10011132

[61413-54-5] SB 95952, ZK 62711
MF: $C_{16}H_{21}NO_3$ **FW:** 275.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A cell-permeable selective PDE4 inhibitor

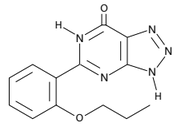
5 mg
10 mg
25 mg



Zaprinast 10010421

[37762-06-4] M&B 22,948, 2-(o-Propoxyphenyl)-8-azapurin-6-one
MF: $C_{13}H_{13}N_5O_2$ **FW:** 271.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥1 year at -20°C
Summary: A cGMP-specific PDE inhibitor that moderately inhibits PDE5 and PDE6 with IC_{50} values of 0.5-0.76 and 0.15 µM, respectively

10 mg
50 mg
100 mg
250 mg



PDE Inhibitors

Item No.	Product Name	Inhibitory Target	Effective Concentration
13183	CP 80633	PDE4	IC_{50} = 1.27 µM
13347	IBMX	Non-specific Inhibitor of cAMP and cGMP PGEs	
13624	Icariin	PDE5	IC_{50} = 5.9 µM
13357	Milrinone	PDE3A PDE3B	IC_{50} = 0.45 µM IC_{50} = 1 µM
10011133	Papaverine	Phophodiesterase activity	IC_{50} = 13 µM
10011132	Rolipram	PDE4	
10010421	Zaprinast	PDE5 PDE6	IC_{50} = 0.5-0.76 µM IC_{50} = 15 µM

PKA, PKC, & PKG Inhibitors

Item No.	Product Name	Target	Effective Concentration
10010249	H-8 (hydrochloride)	PKA PKG	K_i = 1.2 µM K_i = 0.42 µM
13312	H-9 (hydrochloride)	PKA PKC PKG	K_i = 1.9 µM K_i = 18 µM K_i = 0.87 µM
10010556	H-89	PKA	IC_{50} = 0.14 µM
10011011	KT 5720	PKA	K_i = 60 nM
10010965	KT 5823	PKG	IC_{50} = 234 nM
10459	PKC 412	PKCα PKCβ PKCγ	IC_{50}s range from 80-500 nM
13333	Ro 31-7549 (acetate)	PKC	IC_{50} = 158 nM
13334	Ro 31-8220 (mesylate)	PKCα PKCβI PKCβII PKCγ PKCε	IC_{50} = 5 nM IC_{50} = 24 nM IC_{50} = 14 nM IC_{50} = 27 nM IC_{50} = 24 nM

vol. 15 Rs

Thomas G. Brock, Ph.D.

G Proteins and Their Coupled Receptors

At the cell surface, there are receptors that couple with enzymes, like the receptor tyrosine kinases, and there are those that activate transmembrane ion channels. A third family of receptors includes the G protein-coupled receptors (GPCR). These receptors, also known as seven transmembrane receptors because each has seven regions that pass through the plasma membrane, constitute a large family of literally hundreds of human members.[1] Different GPCRs respond to such diverse stimuli as light, volatile compounds, bioactive lipids, cytokines, hormones, and neurotransmitters. Receptor activation puts specific, dedicated G proteins into play, which in turn alters the activity of enzymatic signaling pathways. This article presents different aspects of GPCR action.

Signaling Through the Heterotrimeric G Protein

Signaling begins with activation of the GPCR, typically by binding of an appropriate ligand to a specific ligand binding domain. This domain can be extracellular, as in the metabotropic glutamate receptors, or entrenched in the plasma membrane, as in the GPCRs for the bioactive lipid leukotriene B_4. An interesting group includes the opsins, light-sensitive GPCRs found in photoreceptors of the retina. The opsins themselves are the seven transmembrane proteins, each of which covalently binds a vitamin A-based chromophore linked to a lysine residue in the seventh transmembrane region, within the membrane itself. The absorption of a photon of light causes isomerization of the chromophore, resulting in a conformational change in the opsin protein, just as ligand binding does to other GPCRs. The GPCR can now activate a trimeric GTP-binding protein, or G protein (Figure 1).

The G protein is composed of three protein subunits, Gα, Gβ, and Gγ. Both the Gα and Gγ subunits are post-translationally modified to have covalently attached lipid tails, which anchor the G protein to the plasma membrane. In the resting, unstimulated state, the Gα subunit contains GDP and the G protein is inactive. The inactive G protein may be associated with an inactive receptor or it may only bind after the receptor is activated. In both situations, the activated receptor acts as a guanine nucleotide exchange factor (GEF), inducing the release of GDP from the G protein. GTP, which is abundant in the cytoplasm, replaces the GDP, activating both the Gα subunit and the β/γ complex. In some cases, the activated Gα subunit separates from the β/γ complex, whereas, in other cases, the two activated components remain together. In either case, both of the activated components can now regulate the activity of target proteins in the plasma membrane, including adenylate cyclases, phospholipase C (PLC) isoforms, potassium and calcium ion channels, guanine-nucleotide exchange factors for the GTPase Rho A (RhoGEFs), and other effector enzymes. The activated target proteins then propagate the signal forward to other components in the signaling cascade.

The Gα subunit, in addition to being an intermediary in activating a target protein, is a GTPase, ultimately hydrolyzing its bound GTP to GDP, thus inactivating itself. This step can be accelerated by the binding of another protein, called regulators of G protein signaling (RGS), or, more accurately, GTPase-accelerating proteins (GAP).[2] The inactivated GDP-bound Gα subunit actively recruits specific β/γ complexes, stopping their signaling to re-form an inactive G protein. This G protein can once again interact with the activated receptor to repeat GDP/GTP exchange and signal propagation. Interestingly, some receptors fastidiously activate specific types of G proteins, while other receptors may be described as 'biased' toward a certain G protein or even 'promiscuous' in G protein activation. Ultimately, activated receptors are phosphorylated on cytoplasmic residues by GPCR kinases (GRKs). Phosphorylation promotes high-affinity binding with an arrestin protein, preventing further interaction of the receptor with G proteins. Arrestin binding also targets the receptor for internalization *via* clathrin-coated pits.

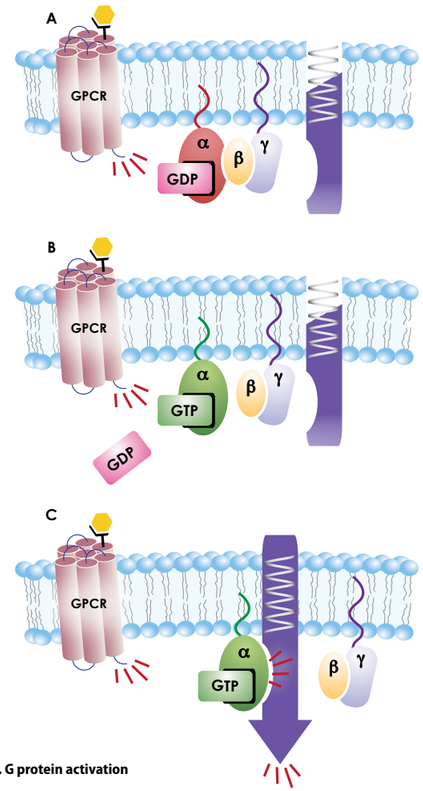


Figure 1. G protein activation

Two Related Examples

The hundreds of unique GPCRs, with their thousands of different ligands, all funnel their actions through G proteins, with the critical component typically being the Gα subunit. As an example, many GPCRs signal exclusively through Gαs, which stimulates the activity of certain forms of adenylate cyclase (ADCY). The ADCY constitute a family of proteins which synthesize cAMP from ATP (Figure 2). If cAMP is not metabolized by phosphodiesterases (PDE), then it can activate two pathways: protein kinase A (PKA) and exchange proteins activated by cAMP (Epac). In resting cells, PKA exists as a tetramer of two regulatory subunits holding two catalytic subunits in an inactive state. The association of cAMP with the regulatory components causes dissociation of the tetramer, allowing the free, active catalytic subunits of the kinase to phosphorylate target proteins.[3] Perhaps most notably, PKA phosphorylates CREB, which binds the cAMP response element (CRE) and alters gene transcription. PKA can also target other transcription factors (*e.g.*, NF-κB, NFAT, RARα), as well as a wide variety of other proteins (*e.g.*, BAD, PLCγ1, histone H3). Interestingly, PKA also phosphorylates inhibitors of protein phosphatases PP1 and PP2A, preventing the dephosphorylation of PKA and non-PKA targets. The Epac proteins represent 2 of 6 human Rap GEFs. By replacing GTP for GDP in Rap, Epacs modulate kinase signaling, mitogenesis, and exocytosis.[4]

On the flip side of this stimulatory pathway is GPCR signaling through an inhibitory subunit, Gαi. Activation of a GPCR that puts $G\alpha_i$

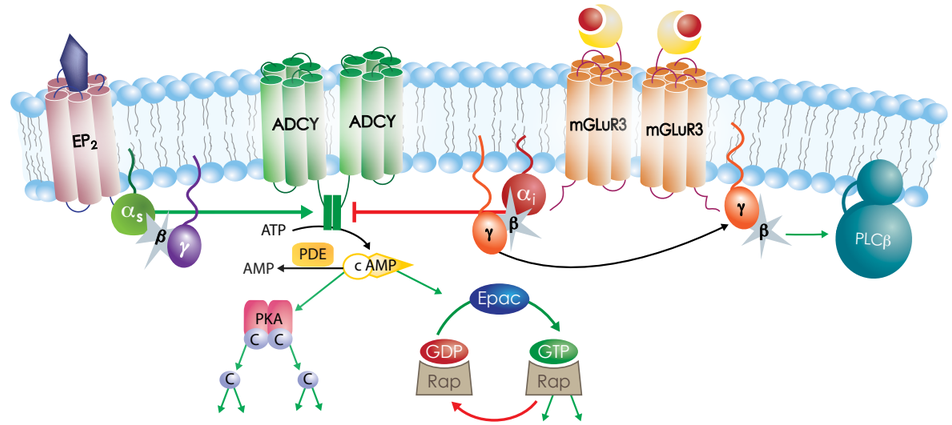


Figure 2. Signaling through a $G\alpha_s$ GPCR, the prostaglandin E_2 receptor EP_2, and a $G\alpha_i$ GPCR, the metabotropic glutamate receptor mGluR3, to adenylate cyclase (ADCY)

in play suppresses the generation of cAMP by ADCY. This can be important in certain cell types that have constitutive activation of ADCY and high basal levels of cAMP. More commonly, $G\alpha_i$-mediated inactivation of ADCY blocks concomitant or subsequent attempts to activate ADCY through $G\alpha_s$-dependent GPCRs. For some reason, the Gβγ dimers which dissociate from $G\alpha_i$ are particularly involved in activating other signaling cascades. Thus, as $G\alpha_i$ is inhibiting cAMP production, its G protein partners may activate certain isoforms of PLC, phosphoinositide 3-kinase, and select ion channels, like the G-protein-regulated inward rectifier K^+ channels. The diversity of effects of different G protein subunits suggests a closer look at each of the distinct subunits is warranted.

G Protein Subunits

In the annotated database UniProtKB/Swiss-Prot (www.uniprot.org), the Gα subunits are grouped into four subfamilies: $G\alpha_s$, $G\alpha_{i/o/t/z}$, $G\alpha_q$, and $G\alpha_{12}$. All Gα subunits have four GTP binding sites and hydrolyze GTP. They are typically N-terminally myristoylated or palmitoylated, which is necessary for membrane association. Most of the 17 human Gα subunits consist of 350-395 aa organized in a globular structure dominated with α helices (Figure 3). A single gene is the source for two major $G\alpha_s$ isoforms, $G\alpha_{s1}$ and $G\alpha_{s2}$, through alternative splicing; an additional extra long (XLas) isoform of 1037 aa is also derived from the same gene. A distinct gene gives rise to an olfactory type $G\alpha_s$ subunit (Golf), which is expressed on chemosensory organs of many organisms.[5] As noted above, G proteins containing the $G\alpha_s$ subunit drives cAMP generation by ADCY. All of the $G\alpha_s$ isoforms can also be activated by cholera toxin,

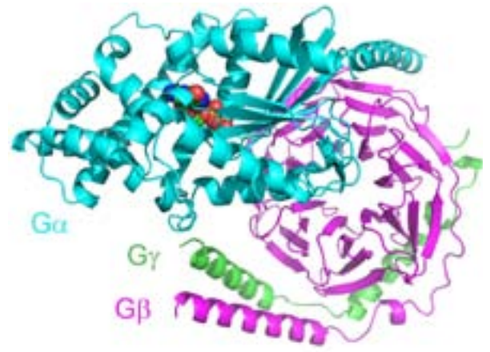


Figure 3. The structure of the heterotrimeric G protein, with GDP bound to Gα (cyan) and Gβ (magenta) linking Gα to Gγ (green)[8]

which induces ADP-ribosylation on a key arginine residue resulting in constitutive activation.

The $G\alpha_{i/o/t/z}$ group includes eight members closely related by structure if not function. As outlined above, the three $G\alpha_i$ members would be expected to inhibit adenylate cyclase, which $G\alpha_{i1}$ and $G\alpha_{i2}$ do. However, $G\alpha_{i3}$, which also goes by the name $G\alpha_k$, stimulates receptor-regulated K^+ channels, even though its sequence is a 98% positive match with $G\alpha_{i1}$. Two of the three $G\alpha_t$, elements of the transducin G protein subunits, couple activation of the rhodopsin receptor by visual impulses with cGMP PDE; $G\alpha_{t1}$ acts in rods and $G\alpha_{t2}$ is in cones.[6] $G\alpha_{t3}$, a component of gustducin, links bitter, sweet, and umami taste sensation with cGMP PDE stimulation. The $G\alpha_o$ and $G\alpha_z$ subunits are involved in diverse receptor pathways but their modes of signaling are obscure. All of these family members, except $G\alpha_z$, are ADP-ribosylated on cysteine residues, and inhibited, by pertussis toxin.

The $G\alpha_q$ subfamily activates phospholipase C (PLC), which converts phosphatidylinositol 4,5-bisphosphate (PIP_2) to diacylglycerol (DAG) and inositol 1,4,5-trisphosphate (IP_3). IP_3 induces the release of calcium from intracellular stores, propagating Ca^{2+}-dependent signaling. Also, Ca^{2+} acts with DAG to turn on certain isoforms of PKC. This family, also referred to as $G\alpha_{q/11}$, includes $G\alpha_{14}$ and $G\alpha_{15}$, as well as $G_{\alpha q}$ and $G\alpha_{11}$. $G\alpha_{15}$ is specifically expressed in hematopoietic cells. Finally, the $G\alpha_{12}$ subfamily has two members, 12 and 13. Both interact with UBX domain-containing protein 11 (UBXN11) to promote the Ras homolog RhoA, a small GTPase that regulates actin reorganization. In addition, $G\alpha_{13}$ binds the integrin α11bβ3 to modulate ligand-integrin signaling through RhoA.[7]

Less is known about the Gβ and Gγ subunits. There are 5 human Gβ proteins of 340-295 aa. Each contains 7 WD repeats, which facilitate forming the G protein trimer (Figure 3). The 12 human Gγ proteins are small, only 67-75 aa. $G\gamma_{T1}$ and $G\gamma_{T2}$ are restricted to transducins in retinal rods and cones, respectively, while $G\gamma_7$ associates with Golf. All are a subject of current research.

References

1. Vassilatis, D.K., Hohmann, J.G., Zeng, H., *et al. Proc. Natl. Acad. Sci. USA* **100(8),** 4903-4908 (2003).
2. Sjögren, B. and Neubig, R.R. *Mol. Pharmacol.* **78(4),** 550-557 (2010).
3. Shabb, J.B. *Chem. Rev.* **101,** 2381-2411 (2001).
4. Patten, C.S., Daniels, D., Suzuki, A., *et al. Regul. Pept.* **142,** 111-122 (2007).
5. Pace, U. and Lancet, D. *Proc. Natl. Acad. Sci. USA* **83,** 4947-4951 (1986).
6. Grant, J.E., Guo, L.-W., Vestling, M.M., *et al. J. Biol. Chem.* **281(10),** 6194-6202 (2006).
7. Gong, H., Shen, B., Flevaris, P., *et al. Science* **327(5963),** 340-343 (2010).
8. Lambright,D.G., Sondek,J., Bohm,A., *et al. Nature* **379,** 311-319 (1996)

Eicosanoid GPCR Signaling

$CysLT_1$ Receptor Polyclonal Antibody 120500

Peptide affinity-purified IgG **Stability:** ≥3 years at -20°C
Summary: Antigen: human $CysLT_1$ receptor C-terminal amino acids 318-337 • Host: rabbit • Cross Reactivity: (+) human $CysLT_1$ receptor • Application(s): FC, ICC, IHC (paraffin-embedded sections), and WB • The $CysLT_1$ receptor binds LTD_4, LTC_4, and LTE_4, playing a major role in asthma by facillitating airway and pulmonary vascular smooth muscle contraction, increased vascular permeability, and stimulating mucus secretion. The mRNA for the human $CysLT_1$ receptor is expressed in spleen and peripheral blood leukocytes with smaller amounts in lung, placenta, and small intestine.

500 µl

•Also Available: **$CysLT_1$ Receptor Blocking Peptide** (320500)

$CysLT_2$ Receptor (C-Term) Polyclonal Antibody 120550

Peptide affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human $CysLT_2$ receptor C-terminal amino acids 330-346 • Host: rabbit • Cross Reactivity: (+) human $CysLT_2$ receptor; (-) $CysLT_1$ receptor, mouse, rat, and ovine $CysLT_2$ receptors • Application(s): FC, IHC, and WB • The $CysLT_2$ receptor binds LTD_4, LTC_4, and LTE_4 playing a major role in asthma by facillitating airway and pulmonary vascular smooth muscle contraction, increased vascular permeability, and stimulating mucus secretion. The mRNA for the human $CysLT_2$ receptor is expressed in lung macrophages, airway smooth muscle, cardiac Purkinje cells, adrenal medulla cells, peripheral blood leukocytes, spleen, placenta, and brain.

1 ea

•Also Available: **$CysLT_2$ Receptor (C-Term) Blocking Peptide** (320550)

$CysLT_2$ Receptor (N-Term) Polyclonal Antibody 120560

Peptide affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human $CysLT_2$ receptor N-terminal amino acids 1-18 • Host: rabbit • Cross Reactivity: (+) human $CysLT_2$ receptor; (-) $CysLT_1$ receptor, mouse, and rat $CysLT_2$ receptors • Application(s): FC, ICC, IHC, and WB • The $CysLT_2$ receptor binds LTD_4, LTC_4, and LTE_4 playing a major role in asthma by facillitating airway and pulmonary vascular smooth muscle contraction, increased vascular permeability, and stimulating mucus secretion. The mRNA for the human $CysLT_2$ receptor is expressed in lung macrophages, airway smooth muscle, cardiac Purkinje cells, adrenal medulla cells, peripheral blood leukocytes, spleen, placenta, and brain.

500 µl

•Also Available: **$CysLT_2$ Receptor (N-Term) Blocking Peptide** (320560)

DP_1 Receptor Polyclonal Antibody 101640

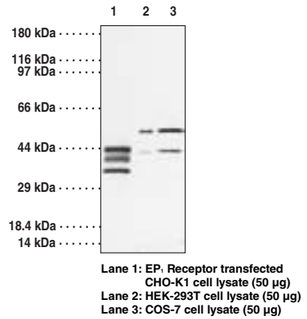
PGD_2 Receptor 1
Peptide affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: mouse DP_1 receptor N-terminal amino acids 2-21 • Host: rabbit • Cross Reactivity: human, mouse, and rat DP_1 receptors • Application(s): ICC and WB • DP_1 receptor is one of two receptor isoforms for PGD_2, a major COX metabolite of arachidonic acid. As a GPCR, the receptor primarily couples to G_s to increase cAMP, but also transiently increases Ca^{2+}, apparently through the cAMP pathway

1 ea

EP_1 Receptor Polyclonal Antibody 101740

PGE_2 Receptor 1
Peptide affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human EP_1 receptor C-terminal amino acids 380-402 • Host: rabbit • Application(s): ICC and WB • Binding of PGE_2 to the EP_1 receptor results in an increase in phosphatidyl inositol turnover with subsequent increase in intracellular free Ca^{2+}. Pharmacologically, EP_1 receptors mediate contraction of smooth muscle.

500 µl
Trial Size



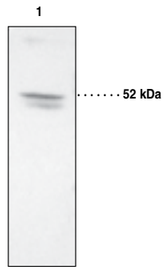
Lane 1: EP$_1$ Receptor transfected CHO-K1 cell lysate (50 µg)
Lane 2: HEK-293T cell lysate (50 µg)
Lane 3: COS-7 cell lysate (50 µg)

•Also Available: **EP_1 Receptor Blocking Peptide** (301740)

EP_2 Receptor Polyclonal Antibody 101750

PGE_2 Receptor 2
Peptide affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human EP_2 receptor C-terminal amino acids 335-358 • Host: rabbit • Cross Reactivity: (+) human, mouse, and rat EP_2 receptors; (-) EP_1, EP_3, and EP_4 receptors • Application(s): ICC and WB • Binding of PGE_2 to the EP_2 receptor results in an increase in adenylate cyclase activity with a subsequent increase in cAMP. Pharmacologically, EP_2 receptors mediate relaxation of smooth muscle and are distinguished from EP_4 receptors by their sensitivity to the EP_2 receptor selective agonist butaprost.

500 µl



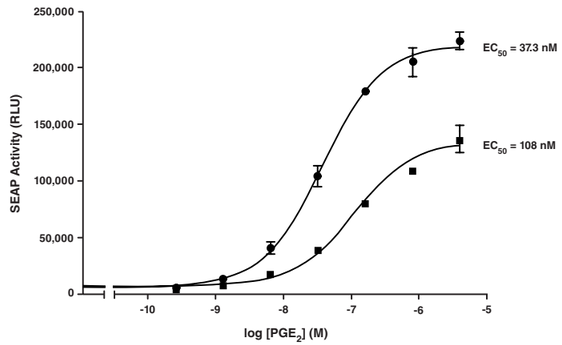
Lane 1: Rat sensory neuron (20 µg)

•Also Available: **EP_2 Receptor Blocking Peptide** (301750)

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

PGE_2 Receptor 2
Stability: ≥1 year at -20°C
Summary: A cell-based screening assay based on novel transfection (STEP) technology

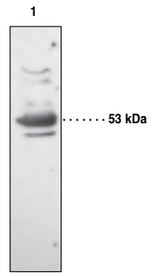
100 tests



EP_3 Receptor Polyclonal Antibody 101760

PGE_2 Receptor 3
Peptide affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human EP_3 receptor amino acids 308-327 • Host: rabbit • Application(s): ICC and WB • As a result of splice variation, the EP_3 receptor can be expressed as multiple isoforms that differ in the length and sequence of their C-terminal tails. The signal transduction mechanism varies depending on the isoform being expressed, implicating the importance of the C-terminal region of the receptor for coupling to G-proteins.

500 µl



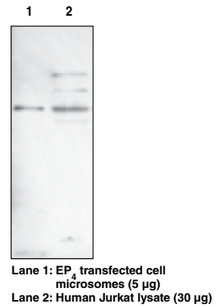
Lane 1: Rat sensory neuron (20 µg)

•Also Available: **EP_3 Receptor Blocking Peptide** (301760)

EP_4 Receptor (C-Term) Polyclonal Antibody 101775

PGE_2 Receptor 4
Peptide affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human EP_4 receptor C-terminal amino acids 459-488 • Host: rabbit • Cross Reactivity: (+) human, mouse, ovine, and rat EP_4 receptors; (-) EP_1, EP_2, and EP_3 receptors • Application(s): ICC, IHC, and WB • Binding of PGE_2 to the EP_4 receptor causes an increase in intracellular cyclic AMP and subsequent relaxation of smooth muscle. In addition to sequence differences, EP_4 receptors are distinguished from EP_2 receptors by their insensitivity to the EP_2 receptor selective agonist butaprost.

500 µl



Lane 1: EP$_4$ transfected cell microsomes (5 µg)
Lane 2: Human Jurkat lysate (30 µg)

•Also Available: **EP_4 Receptor Blocking Peptide** (301775)

EP_4 Receptor (C-Term) Polyclonal PE Antibody 10479

PGE_2 Receptor 4
Peptide affinity-purified IgG-PE **Stability:** ≥1 year at 4°C
Summary: Antigen: human EP_4 receptor C-terminal amino acids 459-488 • Host: rabbit • Cross Reactivity: (+) human, mouse, ovine, and rat EP_4 receptors; (-) EP_1, EP_2, and EP_3 receptors • Application(s): FC and IF • Binding of PGE_2 to the EP_4 receptor causes an increase in intracellular cAMP and subsequent relaxation of smooth muscle. In addition to sequence differences, EP_4 receptors are distinguished from EP_2 receptors by their insensitivity to the EP_2 receptor selective agonist butaprost.

500 µl

EP_4 Receptor (N-Term) Polyclonal Antiserum 101770

PGE_2 Receptor 4
Lyophilized antiserum **Stability:** ≥2 years at -20°C
Summary: Antigen: human EP_4 receptor N-terminal amino acids 1-22 • Host: rabbit • Cross Reactivity: (+) human, ovine, mouse, and rat EP_4 receptors • Application(s): WB • Binding of PGE_2 to the EP_4 receptor causes an increase in intracellular cAMP and subsequent relaxation of smooth muscle. In addition to sequence differences, EP_4 receptors are distinguished from EP_2 receptors by their insensitivity to the EP_2 receptor selective agonist butaprost.

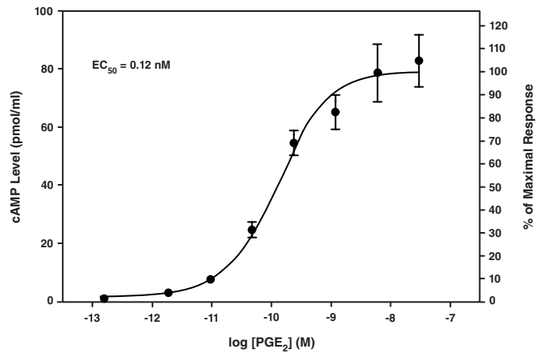
1 ea

•Also Available: **EP_4 Receptor (N-Term) Blocking Peptide** (101780)

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

Stability: ≥1 year at -20°C
Summary: A cell-based screening assay based on novel transfection (STEP) technology

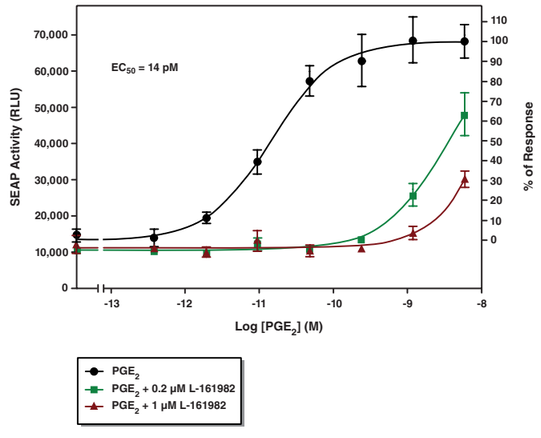
1 ea



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

PGE_2 Receptor 2
Stability: ≥1 year at -20°C
Summary: A cell-based screening assay based on novel transfection (STEP) technology

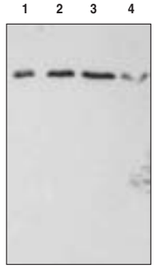
100 tests



FP Receptor Polyclonal Antibody 101802

$PGF_{2\alpha}$ Receptor
Peptide affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: mouse FP receptor amino acids 2-16 • Host: rabbit • Application(s): WB • The FP receptor is a G protein-coupled receptor known to elicit smooth muscle contraction in a variety of tissues. FP receptor mRNA is found in reproductive, gastric, neural, and ocular tissues, as well as, specialized cells of the kidney.

500 µl



Lane 1: Bovine cornea (20 µg)
Lane 2: Bovine cornea (30 µg)
Lane 3: Bovine cornea (40 µg)
Lane 4: Ram seminal vesicle microsomes (30 µg)

•Also Available: **FP Receptor Blocking Peptide** (301802)

IP Receptor (human) Polyclonal Antibody 10005518

PGI_2 Receptor, Prostacyclin Receptor
Peptide affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human IP receptor N-terminal amino acids 1-16 conjugated to KLH • Host: rabbit • Cross Reactivity: (+) human, mouse, and rat IP receptor • Application(s): WB • The IP receptor is a GPCR that mediates the action of PGI_2. It participates in signal transduction of the pain response, cardioprotection, and inflammation.

500 µl

•Also Available: **IP Receptor (human) Blocking Peptide** (10005519)

IP Receptor (mouse) Polyclonal Antibody 160070

PGI_2 Receptor, Prostacyclin Receptor
Peptide affinity-purified IgG **Stability:** ≥2 years at -20°C
Summary: Antigen: mouse IP receptor N-terminal amino acids 3-16 conjugated to KLH • Host: rabbit • Cross Reactivity: (+) mouse and rat IP receptor; (-) human IP receptor • Application(s): WB • The IP receptor is a GPCR that mediates the action of PGI_2. It participates in signal transduction of the pain response, cardioprotection, and inflammation. There is a significant amino-terminal truncation of the human IP receptor compared to the mouse receptor. This antibody is useful only for immunochemical analysis of mouse and rat samples.

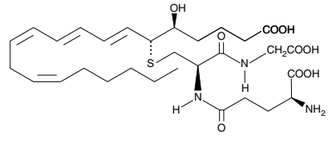
1 ea

•Also Available: **IP Receptor (mouse) Blocking Peptide** (360070)

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

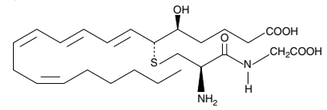


•Also Available: **Leukotriene C_4 Lipid Maps MS Standard** (10007241)

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

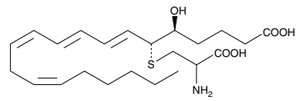
25 µg
50 µg
100 µg
1 mg



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 SRS-A; 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

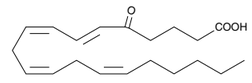
25 µg
50 µg
100 µg
1 mg



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 couples to $G_{i/o}$ to inhibit cyclic AMP production and to mobilize intracellular calcium, enabling chemotaxis for eosinophils and neutrophils.

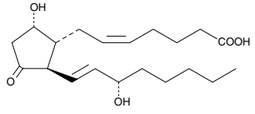
500 µl

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

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

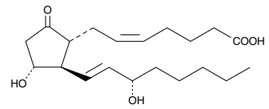


•Also Available: **Prostaglandin D_2 Lipid Maps MS Standard** (10007202)

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

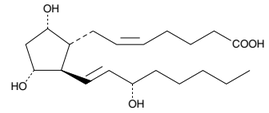


•Also Available: **Prostaglandin E_2 Lipid Maps MS Standard** (10007211)

Prostaglandin $F_{2\alpha}$ 16010

[551-11-1] Dinoprost
MF: $C_{20}H_{34}O_5$ **FW:** 354.5 **Purity:** ≥99%*
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A widely distributed primary PG occuring in many species; causes contraction of vascular, bronchial, intestinal, and myometrial smooth muscle, and also exhibits potent luteolytic activity

1 mg
5 mg
10 mg
50 mg

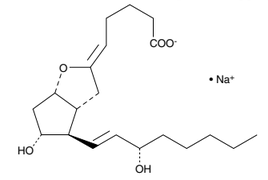


•Also Available: **Prostaglandin $F_{2\alpha}$ Lipid Maps MS Standard** (10007221)

Prostaglandin I_2 (sodium salt) 18220

[61849-14-7] Epoprostenol, Prostacyclin
MF: $C_{20}H_{31}O_5$ • Na **FW:** 374.5 **Purity:** ≥99%*
A crystalline solid **Stability:** ≥1 year at -20°C
Summary: A primary metabolite of arachidonic acid formed by COX and PGI synthase; acts as a potent vasodilator and inhibitor of human platelet aggregation with an IC_{50} value of 5 nM

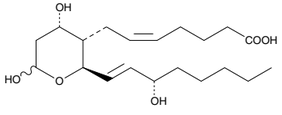
1 mg
5 mg
10 mg
25 mg



Thromboxane B_2 19030

[54397-85-2]
MF: $C_{20}H_{34}O_6$ **FW:** 370.5 **Purity:** ≥99%*
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A stable, biologically inert metabolite formed from the non-enzymatic hydrolysis of TXA_2

1 mg
5 mg
10 mg
50 mg



•Also Available: **Thromboxane B_2-d_4** (319030)
Thromboxane B_2 Lipid Maps MS Standard (10007237)
Thromboxane B_2 Quant-PAK (10006832)

TP Receptor (human) Polyclonal Antibody 10004452

TXA_2 Receptor
Peptide affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human TP receptor C-terminal amino acids 323-343 • Host: rabbit • Cross Reactivity: (+) human, mouse, rat, and Cos-7 (African green monkey) TP receptor • Application(s): ICC and WB • The TP receptor is a GPCR that mediates the action of TXA_2.

500 µl

•Also Available: **TP Receptor (human) Blocking Peptide** (10009368)

TP Receptor (human) Polyclonal FITC Antibody 10012559

TXA_2 Receptor
Peptide affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human TP receptor C-terminal amino acids 323-343 • Host: rabbit • Cross Reactivity: (+) human, mouse, rat, and Cos-7 (African green monkey) TP receptor • Application(s): FC, IF, and WB • The TP receptor is a GPCR that mediates the action of TXA_2.

500 µl

TP Receptor (mouse) Polyclonal Antibody 101882

TXA_2 Receptor
Affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: mouse TP receptor amino acids 275-289 • Host: rabbit • Cross Reactivity: (+) human, mouse, rat, Cos-7 (African green monkey), and bovine TP receptor (able to detect both TP_A and TP_B isoforms) • Application(s): IHC (formalin-fixed paraffin embedded sections) and WB • The TP receptor is a GPCR that mediates the action of TXA_2.

500 µl

•Also Available: **TP Receptor (mouse) Blocking Peptide** (10004110)

Eicosanoid Receptors

Receptor	Antibodies	Agonists	Antagonists
DP_1	**DP_1 Receptor Polyclonal Antibody** 101640	**Prostaglandin D_2** 12010, **BW 245C** 12050, **15(S)-15-methyl Prostaglandin D_2** 12730, **15-deoxy-$\Delta^{12,14}$-Prostaglandin D_2** 12700	**BW A868C** 12060, **AH 6809** 14050, **MK 0524** 10009835, **CAY10471** 10006735
DP_2		**Prostaglandin D_2** 12010, 10118, **15(R)-15-methyl Prostaglandin D_2** 12720, **11-deoxy-11-methylene-15-keto Prostaglandin$_2$** 12415,**13,14-dihydro-15-keto Prostaglandin$_2$** 12610, **15-deoxy-$\Delta^{12,14}$-Prostaglandin J_2** 18570, **Prostaglandin J_2** 18500,**15-deoxy-$\Delta^{12,14}$-Prostaglandin J_2-2-glycerol** 10010132, **Δ^{12}-Prostaglandin J_2** 18550, **15-deoxy-$\Delta^{12,14}$-Prostaglandin D_2** 12700, **Indomethacin** 70270, **11-keto Fluprostenol** 16783	**BAY-u3405** 10156, **CAY10471** 10006735, **CAY10597** 10012539, **GW 848687X** 10010410, **SC-51089** 10011561, **SC-51322** 10010744, **CAY10595** 10012553
EP_1	**EP_1 Receptor Polyclonal Antibody** 101740	**Prostaglandin E_2** 14010, **17-phenyl trinor Prostaglandin E_2** 14810, **17-phenyl trinor 8-*iso* Prostaglandin E_2** 10007931	**AH 6809** 14050, **SC-19220** 14060, **ONO-8711** 14070, **GW 848687X** 10010410
EP_2	**EP_2 Receptor Polyclonal Antibody** 101750 **EP_2 Receptor PE Polyclonal Antibody** 10477	**Prostaglandin E_2** 14010, **Butaprost** 13740, **11-deoxy-16,16-dimethyl Prostaglandin E_2** 14570, **19(R)-hydroxy Prostaglandin E_2** 14910, **CAY10408** 13747, **Misoprostol** 13820	**AH 6809** 14050
EP_3	**EP_3 Receptor Polyclonal Antibody** 101760	**Prostaglandin E_2** 14010, **Sulprostone** 14765, **17-phenyl trinor Prostaglandin E_2** 14810, **11-deoxy-16,16-dimethyl PGE_2** 14570, **17-phenyl trinor 8-*iso* PGE_2** 10007931, **Misoprostol** 13820	**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) PE Polyclonal Antibody** 10479	**Prostaglandin E_2** 14010, **CAY10580** 16835, **L-902,688** 10007712, **CAY10598** 13281, **Misoprostol** 13820	**L-161, 982** 10011565 **GW 627368X** 10009162 **AH 23848** 19023
FP	**FP Receptor Polyclonal Antibody** 101802	**CAY10509** 10009167, **CAY10510** 10009168, **Prostaglandin $F_{2\alpha}$** 16010, **Latanoprost** 16812, 16811, **Bimatoprost** 16820, **17-phenyl trinor Prostaglandin F2α** 16810, **Fluprostenol** 16767, 16768, 16769, **Cloprostenol** 16764, **(±) Cloprostenol** 16765, 16766, 10006692,**15(S)-15-methyl-Prostaglandin $F_{2\alpha}$** 16743, 16750, 16814, 10010839, 16760, **Tafluprost** 10005440, 10005439	**AL 8810** 16735 **AL 8810 isopropyl ester** 10113, **$PGF_{2\alpha}$ dimethyl amide** 16032, **$PGF_{2\alpha}$ dimethyl amine** 16033
IP	**IP Receptor (mouse) Polyclonal Antibody** 160070 **IP Receptor (human) Polyclonal Antibody** 10005518	**Prostaglandin I_2** 18220, **Ciprostene** 18216, **Iloprost** 18215, 10008585, **Beraprost** 18230, **NS-304** 10010411, **13,14-dehydro-15-cyclohexyl Carbaprostacyclin** 18212, **Carbaprostacyclin** 18210, 18211, **Treprostinil** 10162, **MRE-269** 10010412, **Taprostene (free acid)** 10011348, **Cicaprost** 16831, **AFP 07 (free acid)** 13626	**CAY10441** 10005186, **CAY10449** 10005913
TP	**TP Receptor (human) Polyclonal FITC Antibody** 10012559 **TP Receptor (human) Polyclonal Antibody** 10004452 **TP Receptor (mouse) Polyclonal Antibody** 101882	**U-46619** 16450, 10010522, **I-BOP** 19600, **U-44069** 16440 **Carbocyclic Thromboxane A_2** 19010,	**SQ 29,548** 19025, **BAY-u3405** 10156, **I-SAP** 19021, **Pinane Thromboxane A_2** 19020, 10008510, **CAY10471** 10006735, **GW 627368X** 10009162, **BM 567** 10155, **CAY10535** 10010396, **AH 23848** 19023, **L-655,240** 10011562
BLT_1	**BLT_1 Receptor Polyclonal Antiserum** 100019 **BLT_1 Receptor Monoclonal Antibody** 120111 **BLT_1 Receptor Polyclonal Antibody** 120114	**Leukotriene B_4** 20110, **20-trifluoro LTB_4** 20195, **20-hydroxy Leukotriene B_4** 20190, **Leukotriene B_4-3-aminopropylamide** 20114	**U-75302** 70705, **LY223982** 10010024, **Leukotriene B_4 Ethanolamide** 20112, 20115, **14,15-dehydro Leukotriene B_4** 20150, **LY293111** 10009768
BLT_2	**BLT_2 Receptor Polyclonal Antibody** 120124	**Leukotriene B_4** 20110, **CAY10583** 10012424, **20-hydroxy Leukotriene B_4** 20190, **Leukotriene B_4-3-aminopropylamide** 20114	**LY255283** 70715
$CysLT_1$	**$CysLT_1$ Receptor Polyclonal Antibody** 120500	**Leukotriene C_4** 20210, **Leukotriene D_4** 20310, **Leukotriene E_4** 20410, **N-methyl Leukotriene C_4** 13390	**MK 571 (sodium salt)** 70720, **BAY-u9773** 70770, **Zafirlukast** 10008282, **Montelukast** 10008318, **Pranlukast** 10008319, **LY171883** 70710, **REV 5901** 70600
$CysLT_2$	**$CysLT_2$ Receptor (C-Term) Polyclonal Antibody** 120550 **$CysLT_2$ Receptor (N-Term) Polyclonal Antibody** 120560	**Leukotriene C_4** 20210, **Leukotriene D_4** 20310, **Leukotriene E_4** 20410	**BAY-u9773** 70770, **REV 5901** 70600, **HAMI3379** 10580, **BayCysLT2** 10532

vol. 15 Rs

Thomas G. Brock, Ph.D.

The Wonderful World of Wnt Signaling

Wnt's world is complex, colorful, and compelling. Perhaps a dozen different forms of Wnt itself are produced and delivered to neighboring cells, where they control such complex processes as embryogenesis, heart, eye, and neural development, and stem cell renewal. Downstream mutations produce interesting phenotypes in flies (*e.g.*, shaggy, disheveled, armadillo) or less appealing ones in human (*e.g.*, cancer, obesity).[1-3] Wnt's focus on immature cells means that Wnt is important not only in the first baby steps of development but also in such crossroads as epithelial-mesenchymal transition and stem cell senescence, processes that maintain their value throughout life. In addition, the Wnt signaling pathway is elegantly complex. The canonical pathway will be presented, here, first in a simpler form in human terms and then more completely in the fly.

Canonical Wnt Signaling in Humans

The centerpiece of Wnt signaling is the canonical Wnt/β-catenin pathway. In short, Wnt proteins bind to Frizzled receptors and inhibit the degradation of β-catenin, allowing β-catenin-dependent gene expression (Figure 1). There is, however, much more to the story. For example, the catenins (α and β) normally play essential roles at cell-cell adherens junctions, linking cadherins to actin filaments and maintaining cell-cell adhesion. In the absence of Wnt, excess β-catenin is rapidly degraded through a proteasome-dependent process. β-catenin binds to axin, which acts as a scaffolding protein, pulling together the central components needed to mark β-catenin for removal. Joining this complex are the tumor suppressor adenomatous polyposis coli (APC), casein kinase 1α (CK1α), and glycogen synthase kinase-3β (GSK3β). Phosphorylation of β-catenin on Ser^{45} by CK1 primes for subsequent and sequential phosphorylation on Ser^{33}, Ser^{37}, and Thr^{41} by GSK3β. This enables binding of β-catenin by the substrate recognition protein βTrCP of the Skp1, Cul1, F-box protein (SCF) E3 ubiquitin ligase complex, which catalyzes ubiquitination that is necessary for proteasomal degradation. In the absence of β-catenin, transducin-like enhancer proteins (TLE) bind to the transcriptional activator TCF, inhibiting gene expression. The transcriptional corepressor TLE also serves as a docking site for histone deacetylatses (HDAC), which remove acetyl groups from chromatin to silence transcription.

In the presence of Wnt, β-catenin breakdown is avoided. The seven-transmembrane Frizzled (Fzd) receptors include seven members which require a co-receptor, one of two low density lipoprotein receptor-related proteins (LRP), either LRP5 or LRP6. In response to Wnt-induced assembly of the Fzd-LRP5/6 complex, dishevelled (Dvl) proteins bind to the cytoplasmic C-terminus of the Frizzled receptor, leading to the recruitment of Axin-GSK3β. The dual phosphorylation of a cytoplasmic PPPSPAT motif on LRP by CK1 and GSK3β stabilizes Axin binding to LRP. Unphosphorylated β-catenin accumulates in the cytoplasm and, subsequently, within the nucleus, with nuclear β-catenin binding to TCF, displacing TLE. β-catenin, then, acts as a co-activator, in concert with the histone acetyltransferases CBP and p300, to induce the transcription of Wnt target genes.

Importantly, failure to phosphorylate β-catenin in the absence of Wnt allows β-catenin to escape degradation, move to the nucleus, and alter transcription. This can be important in carcinogenesis. A lack of β-catenin phosphorylation may result from mutations to β-catenin that prevent its targeting by CK1α or GSK3β, suppression or inactivation of these kinases, or defects in scaffold formation. Also, several kinases (Akt, p70S6K, PKC) can phosphorylate GSK3β on Ser^{9}, directly inhibiting its ability to phosphorylate targets like β-catenin.

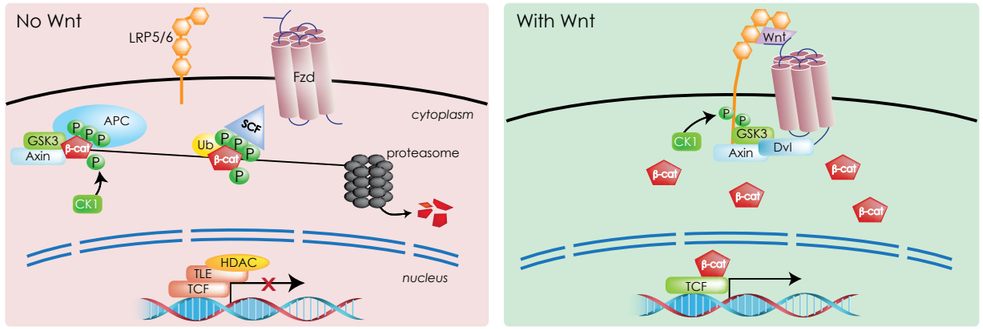


Figure 1. Canonical Wnt signaling

Wnt Signaling in *Drosophila*

In the fruit fly, a wingless phenotype was traced to one gene, subsequently designated *wingless (wg)*. Its product was found to be homologous to the Wnt-1 vertebrate proto-oncogene.[4] Mutations of *wg* and the six related Wnt isoforms in fly have demonstrated that this pathway is involved in diverse spatially and temporally discrete functions, from the establishment of imaginal disc primordia in larvae to the patterning of wing marginal cells.[5,6] The canonical Wnt pathway in *Drosophila* is nicely summarized in KEGG, the Kyoto Encyclopedia of Genes and Genomes (www.genome.jp/kegg/kegg1.html), which is adapted here to extend our understanding (Figure 2).

The Wnts are a secreted morphogen. However, before secretion, they are palmitoylated by protein-cysteine N-palmitoyltransferase (porcupine, PORC), as well as glycosylated.[7] These post-translational modifications serve to limit their distribution by positioning them on immediately-neighboring cells. Wnt signaling can be blocked by extracellular antagonists. Wnt inhibitory factor-1 (Wif-1) and secreted Frizzled-related proteins (FRP) primarily bind to Wnt. The Wnt interaction with LRP co-receptors is prevented by Dickkopf (Dkk) proteins. Wif-1, 5 different FRP isoforms, and 4 Dkk proteins must be secreted in a way that modulates the actions of the several Wnt isoforms during development. Each protein, however, also represents a point of dysfunction that may contribute to aberrant morphogenesis or disease.

As noted earlier, Axin provides a scaffold upon which β-catenin (armadillo, *arm*, in fly) is phosphorylated by CK1α and GSK3β (shaggy, *sgg*, in fly) en route to proteasomal degradation. Dvl (*dsh* in fly) can associate with, and inhibit GSK3β bound to Axin; association is facilitated by guanylate binding proteins (GBP) and inhibition is furthered by phosphorylation of Dvl by CK1ε.[8] A CXXC-type zinc finger protein, Idax, can bind DvL and prevent its association with Axin and inhibition of GSK3β. The protein naked cuticle (nkd) promotes Dvl degradation, antagonizing Wnt signaling. APC plays an important role by binding and blocking protein phosphatase 2A (PP2A) from accessing β-catenin: without APC, PP2A dephosphorylates terminal sites on β-catenin, removing the SCF recognition site and preventing ubiquitination and degradation.[9] Away from Axin, APC associates with Siah-1, Siah-1-interacting protein (SIP), Skp1, and transducin β-like 1 (TBL1) to form SCF-like complex. Genotoxic stresses (*e.g.*, UV-induced DNA damage) activates p53,

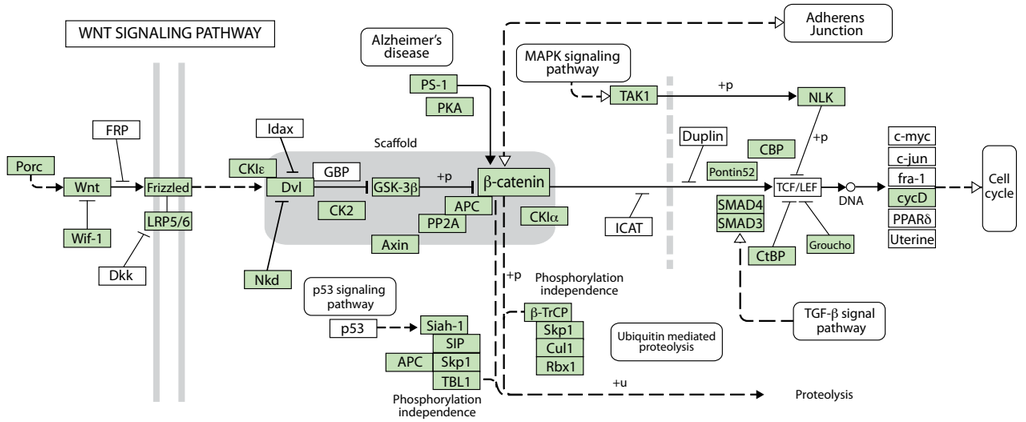


Figure 2. A KEGG diagram of the canonical Wnt/β-catenin pathway. Boxes in green indicate proteins relevant to Wnt signaling in *Drosophila melanogaster*. White boxed proteins are restricted to vertebrates.

which directly induces Siah-1 expression, allowing formation of the SCF-like complex. This complex ubiquitinates unphosphorylated β-catenin, driving proteasomal degradation.[10]

Interestingly, KEGG notes the link between Wnt/β-catenin signaling and Alzheimer's disease, although Alzheimer's is not a fruit fly disease. The role of Wnt/β-catenin in human pathology, however, is unclear. On the one hand, presenilin (PS-1, which does occur in fly), as a component of the γ-secretase complex, can cleave E-cadherin in response to calcium influx, releasing β-catenin and providing a protective effect through increased Wnt signaling.[11] Also, PS-1 activates phosphatidylinositol 3-kinase and Akt, which inhibit GSK3[12] and should reduce β-catenin turnover. On the other hand, PS-1 can also act as a scaffold where (cAMP-dependent) PKA, instead of CK1α, initiates phosphorylation of β-catenin, allowing GSK3β to complete N-terminal phosphorylation for ubiquitination and degradation.[13] Thus, the role of Wnt in Alzheimer's may depend on a variety of factors.

In mammals, β-catenin-interacting protein (inhibitor of β-cat; ICAT) prevents the interaction between β-catenin and TCF (pangolin, or *pan*, in fly); the same interaction is inhibited by acetylation of TCF within the nucleus by CREB-binding protein (CBP). Both actions block Wnt signaling. Duplin (chromodomain-helicase-DNA-binding protein 8; CHD8, mammals only) can be recruited specifically to the promoter regions of several β-catenin responsive genes, blocking expression. Pontin52, and its interacting partner Reptin52 (corresponding to Tip49a and Tip49b in vertebrates), are ATP-dependent DNA helicases which interact with β-catenin and TCF, altering transcription.[14] Downstream of MAP3K7 (also known as TGF-β-activated kinase 1, or TAK1) is Nemo-like kinase (NLK), which binds to and phosphorylates TCF and LEF, promoting their dissociation from DNA and inhibiting β-catenin-dependent transcription.[15] TGF-β signaling also intersects with the Wnt pathway through Smad proteins: Smads can block the phosphorylation of β-catenin by GSK3β, and β-catenin can partner with Smads to form activator complexes, increasing the transcription of genes of mutual interest, such as PAI-1 and smooth muscle actin.1,[16] Finally, the C-terminal-binding protein (CtBP) is a transcriptional co-repressor which binds a consensus motif on the C-terminus of numerous repressors, including (in fly) hairy, knirps, and snail or (in man) FOXP2, HDAC4, and PRDM16. The interaction of CtBP with the repressor complex formed in the absence of Wnt helps block transcription.[17] Groucho is the fly equivalent of TLE, which was described earlier as central to transcriptional repression.

Non-Canonical Wnt Signaling

Wnt proteins can initiate pathways other than that involving β-catenin. For example, Wnt can act through Ror receptor tyrosine kinases (RTK), inhibiting β-catenin/TCF signaling while activating Rac/Jnk, RhoA/ROCK, and RhoB/Rab4, or it may bind another RTK, Ryk, and signal through Src. Wnt binding to Frizzled without LRP5/6 can drive phospholipase C (PLC) hydrolysis of PIP_2, releasing streams through Ca^{2+}, calmodulin, and calmodulin kinase (CamK), as well as through DAG and PKC. More information is available through recent reviews.[18,19]

Product	Properties and Characteristics
CHIR99021 (13122)	Inhibits GSK3α and GSK3β
BIO (13123)	Reversible inhibitor of GSK-3α/β
XAV939 (13596)	Inhibitor of tankyrase (TNKS) 1 and 2
IWR-1-endo (13659)	a potent inhibitor of the Wnt response
IWR-1-exo (13598)	A diastereomer of IWR-1-endo
Demethoxycurcumin (10961)	Down-regulates the transcriptional coactivator p300
Bisdemethoxycurcumin (10960)	Down-regulates the transcriptional coactivator p300
GSK3β (Phospho-Ser^{9}) Polyclonal Antibody (10009374)	plays a key inhibitory role in both the insulin and Wnt signaling pathways
β-Catenin Polyclonal Antibody (100029)	plays an essential role in development and carcinogenesis
β-Catenin (Phospho-$Ser^{33,37}$) Polyclonal Antibody (10009180)	promotes the ubiquitylation

References

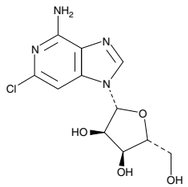
1. Fuxe, J., Vincent, T., and de Herreros, *A.G. Cell Cyle* **9(12),** 2363-2374 (2010).
2. Incassati, A., Chandramouli, A., Eelkema, R. , *et al. Breast Cancer Res.* **12,** 1-14 (2010).
3. Laudes, M. *J. Mol. Endocrinol.* **46(2),** R65-R72 (2011).
4. Rijsewijk, F., Schuermann, M., Wagenaar, E., *et al. Cell* **50,** 649-657 (1987).
5. Cohen, S.M. *Nature* **343,** 173-177 (1990).
6. Couso, J.P., Bishop, S.A., and Arias, A.M. *Development* **120,** 621-636 (1994).
7. Kurayoshi, M., Yamamoto, H., Izumi, S., *et al. Biochem. J.* **402,** 515-523 (2007).
8. del Valle-Pérez, B., Arqués, O., Vinyoles, M., *et al. Mol. Cell. Biol.* **31(14),** 2877-2888 (2011).
9. Su,Y., Fu,C., Ishikawa,S., *et al. Mol. Cell* **32,** 652-661 (2008).
10. Dimitrova, Y.N., Li, J., Lee, Y.-T., *et al. J. Biol. Chem.* **285(18),** 13507-13516 (2010).
11. Boonen, R.A.C.M., van Tijn, P., and Zivkovic, D. *Ageing Res. Rev.* **8,** 71-82 (2009).
12. Baki, L., Shioi, J., Wen, P., *et al. EMBO J.* **23(13),** 2586-2596 (2004).
13. Kang, D.E., Soriano, S., Xia, X., *et al. Cell* **110,** 751-762 (2002).
14. Bauer, A., Chauvet, S., Huber, O., *et al. EMBO J.* **19(22),** 6121-6130 (2000).
15. Li, M., Wang, H., Huang, T., *et al. J. Biol. Chem.* **285(18),** 13397-13404 (2010).
16. Hoover, L.L. and Kubalak, S.W. *Sci. Signal.* **1(46),** 1-6 (2008).
17. Fang, M., Li, J., Blauwkamp, T., *et al. EMBO J.* **25,** 2735-2745 (2006).
18. Camilli, T.C. and Weeraratna, A.T. *Biochem. Pharmacol.* **80(5),** 702-711 (2010).
19. Katoh, M. *Curr. Pharm. Biotechnol.* **12,** 160-170 (2011).

Miscellaneous GPCR Signaling

2-chloro-3-Deazaadenosine 9000787

[40656-71-1] 6-Amino-2-chloropurine riboside, 2-CADO, NSC 158900
MF: $C_{11}H_{13}ClN_4O_4$ **FW:** 300.7 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A stable analog of adenosine that acts as an agonist for adenosine receptors (K_i = 0.3, 0.08, 25.5, and 1.9 µM for A_1, A_{2A}, A_{2B}, and A_3 receptors, respectively); modulates neurotransmission release and blocks seizures by activating adenosine receptors

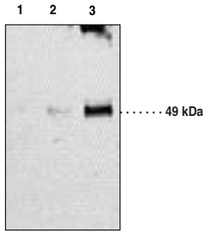
1 mg
5 mg
10 mg



Adenosine Receptor A_{2A} Monoclonal Antibody (Clone 7FG-G5-A2) 10011454

$A_{2A}R$
Affinity-purified IgG_{2a} **Stability:** ≥1 year at -20°C
Summary: Antigen: human full length $A_{2A}R$; the antibody recognizes amino acids 213-220 as determined by epitope mapping • Host: mouse, clone 7FG-G5-A2 • Cross Reactivity: (+) human $A_{2A}R$ • Application(s): WB • $A_{2A}R$ is a multi-pass membrane protein found primarily in the brain striatum, but also in immune cells and other tissues and may play a role in the treatment of Parkinson's disease.

1 ea



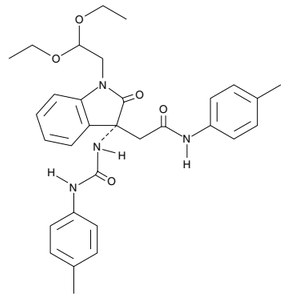
Lane 1: $A_{2A}R$ transfected HEK Cell Membrane Fraction (6.5 µg)
Lane 2: $A_{2A}R$ transfected HEK Cell Membrane Fraction (13 µg)
Lane 3: $A_{2A}R$ transfected HEK Cell Membrane Fraction (26 µg)

•Also Available: **Adenosine Receptor A_{2A} Blocking Peptide** (10092)

AG-041R 10010129

[199800-49-2]
MF: $C_{31}H_{36}N_4O_5$ **FW:** 544.7 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent CCK_B/gastrin receptor antagonist that exhibits selective binding for CCK_B compared to CCK_A; exhibits synergistic inhibitory effects on the cell viability of human gastric cancer cells when administered in combination with the selective COX-2 inhibitor NS-398

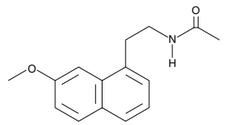
1 mg
5 mg
10 mg
50 mg



Agomelatine 13203

[138112-76-2] Valdoxan®
MF: $C_{15}H_{17}NO_2$ **FW:** 243.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A melatonin receptor MT_1 and MT_2 agonist and competitive antagonist of human and porcine 5-HT_{2C} receptors (pK_i = 6.2 and 6.4, respectively) as well as human 5-HT_{2B} receptors (pK_i = 6.6)

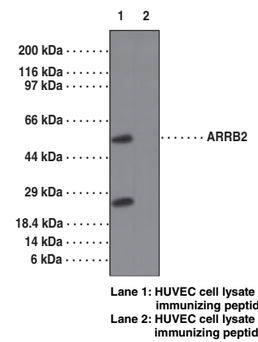
5 mg
10 mg
50 mg
100 mg



ARRB2 Polyclonal Antibody 13498

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

1 ea

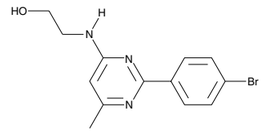


Lane 1: HUVEC cell lysate (Absence of immunizing peptide)
Lane 2: HUVEC cell lysate (Presence of immunizing peptide)

AS-1269574 10626

[330981-72-1]
MF: $C_{13}H_{14}BrN_3O$ **FW:** 308.2 **Purity:** ≥98%
A solution in ethanol **Stability:** ≥1 year at -20°C
Summary: An agonist of GPR199 that is effective both in isolated cells and *in vivo*; increases cAMP levels in HEK293 cells transfected with human GPR119 (EC_{50} = 2.5 µM) and promotes glucose-stimulated insulin secretion in mice (100 mg/kg)

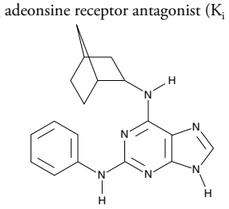
1 mg
5 mg
10 mg
25 mg



CAY10498 10007955

[863202-33-9] 2-phenyl-amino-N6-endo-norbornyladenine
MF: $C_{18}H_{20}N_6$ **FW:** 320.4 **Purity:** ≥98%
A solution in ethanol **Stability:** ≥1 year at -20°C
Summary: A potent and selective A_3 adeonsine receptor antagonist (K_i = 37 nM)

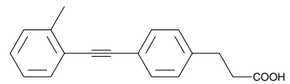
100 µg
500 µg
1 mg
5 mg



CAY10587 13143

[1082058-99-8]
MF: $C_{18}H_{16}O_2$ **FW:** 264.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A selective FFA_1/GPR40 agonist (EC_{50} = 32 nM) that does not exhibit activity on the related FFA receptors FFA_2/GPR43 or FFA_3/GPR41; increases glucose-stimulated insulin secretion at a concentration of 100 nM in rat

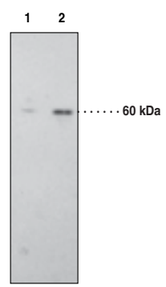
1 mg
5 mg
10 mg
25 mg



CB_1 Receptor Polyclonal Antibody 101500

Peptide affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human, rat, and mouse CB_1 receptor amino acids 1-14 • Host: rabbit • Application(s): WB (does not work for IHC on frozen-tissue sections) • This antisera has been raised against the N-terminal (amino acids 1-14) extracellular region of the of the CB_1 receptor, a receptor localized mainly in the brain and binds the active component of cannabis, Δ^9-tetrahydrocannabinol.

500 µl
Trial Size



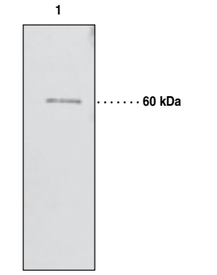
Lane 1: Rat brain homogenate (50 µg)
Lane 2: Rat brain homogenate (100 µg)

•Also Available: **CB_1 Receptor Blocking Peptide** (301500)

CB_1 Receptor (C-Term) Polyclonal Antibody 10006590

Peptide affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human CB_1 receptor amino acids 461-472 • Host: rabbit • Cross Reactivity: human, rat, and mouse CB_1 receptor • Application(s): IHC (parrafin-embedded sections) and WB • This antibody has been raised against the C-terminal (amino acids 461-472) intracellular region of the human CB_1 receptor, a GPCR that binds the active component of cannabis, Δ^9-tetrahydrocannabinol.

500 µl
Trial Size



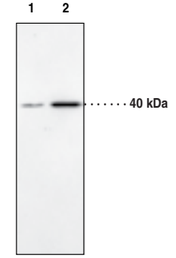
Lane 1: Human cerebellum (30 µg)

•Also Available: **CB_1 Receptor (C-Term) Blocking Peptide** (10006591)

CB_2 Receptor Polyclonal Antibody 101550

Peptide affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human CB_2 receptor amino acids 20-33 • Host: rabbit • Cross Reactivity: (+) human and mouse CB_2 • Application(s): IHC and WB • This antibody has been raised against a sequence between the N-terminus and the first transmembrane domain of the protein of the human CB_2 receptor, a receptor localized predominantly in peripheral tissues, including the spleen and hemopoietic cells and binds the active component of cannabis, Δ^9-tetrahydrocannabinol, as well as anandamide.

500 µl
Trial Size



Lane 1: Jurket (human T-cell leukemia) lysate (50 µg)
Lane 2: Jurket (human T-cell leukemia) lysate (100 µg)

•Also Available: **CB_2 Receptor Blocking Peptide** (301550)

CB_2 Receptor Polyclonal FITC Antibody 10010712

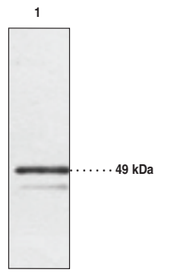
Peptide affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human CB_2 receptor amino acids 20-33 • Host: rabbit • Cross Reactivity: (+) human and mouse CB_2 receptor • Application(s): FC, IF, and WB • This antibody has been raised against a sequence between the N-terminal and the first transmembrane domain of the protein of the human CB_2 receptor, a GPCR that binds the active component of cannabis, Δ^9-tetrahydrocannabinol, as well as anandamide.

500 µl

Chemokine-Like Receptor 1 Polyclonal Antibody 10325

CMKLR1, DEZ, GPCR ChemR23, Resolvin E1 Receptor
Peptide affinity-purified IgG **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. Chemerin, or TIG2, and Resolvin E1 are ligands for this receptor.

500 µl



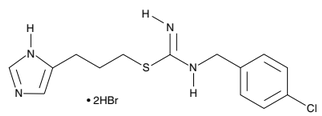
Lane 1: COS-1 cell lysate (10 µg)

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

Clobenpropit (hydrobromide) 10011126

[145231-35-2] Carbamimidothioic Acid, VUF-9153
MF: $C_{14}H_{17}ClN_4S$ • 2HBr **FW:** 470.7 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A selective histamine H_3 receptor antagonist that crosses the blood-brain barrier; inhibits histamine binding in rat brain with an ED_{50} value of 10.5 mg/kg

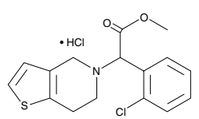
1 mg
5 mg
10 mg
25 mg



(±)-Clopidogrel (hydrochloride) 13657

[90055-48-4]
MF: $C_{16}H_{16}NO_2S$ • HCl **FW:** 358.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An antithrombic compound whose active metabolite is a selective, irreversible antagonist of the platelet purinergic $P2Y_{12}$ receptor (IC_{50} = 100 nM); inhibits ADP-induced platelet aggregation *ex vivo*; shown to be beneficial in the prevention of vascular ischemic events for patients without deficiencies in CYP2C19-related metabolism

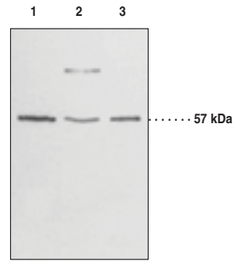
10 mg
50 mg



GPR17 (C-Term) Polyclonal Antibody 10136

G Protein-Coupled Receptor 17
Peptide affinity-purified IgG **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 recognizes signals from both nucleotides and CysLTs. GPR17 is upregulated upon ischemic injury, and its inhibition has been shown to decrease ischemic damage.

500 µl



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

•Also Available: **GPR17 (C-Term) Blocking Peptide** (10345)

GPR35 Polyclonal Antibody 10007660

GPCR35, G Protein-Coupled Receptor 35
Peptide affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: GPR35 amino acids 295-304 • Host: rabbit • Cross Reactivity: (+) human, mouse, and porcine GPR35 • Application(s): IHC (paraffin-embedded sections) and WB • GPR35 ligands include kynurenic acid and zaprinast. Multiple isoforms of this receptor have been reported and GPR35 mRNAs were detected in several tissues including intestine, lymphocytes, skeletal muscle, pancreatic β cells, and tumor cell lines.

500 µl

•Also Available: **GPR35 Blocking Peptide** (10007661)

GPR40 Polyclonal Antibody 10007205

FFAR1, Free Fatty Acid Receptor, G Protein-Coupled Receptor 40
Peptide affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human GPR40 amino acids 210-222 • Host: rabbit • Cross Reactivity: (+) human GPR40 • Application(s): IHC (paraffin-embeded sections) • GPR40 is a GPCR found predominantly in the β-cells of pancreatic islets that has been implicated in the regulation of insulin secretion. Overexpression of GPR40 in mouse β cells leads to glucose intolerance suggesting a link between GPR40 expression and diabetes.

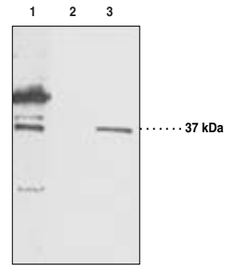
500 µl

•Also Available: **GPR40 Blocking Peptide** (10007206)

GPR55 Polyclonal Antibody 10224

G Protein-Coupled Receptor 55
Peptide affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human GPR55 amino acids 207-219 • Host: rabbit • Cross Reactivity: (+) human, bovine, and mouse GPR55 • Application(s): FC, ICC, and WB • GPR55 is a GPCR identified as a novel cannabinoid receptor that binds THC, anandamide, methanandamide, JWH 015, and many other cannabinoid ligands. This receptor is widely expressed in the brain, specifically found in large dorsal root ganglion neurons.

500 µl



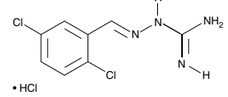
Lane 1: Bovine cornea (5 µg)
Lane 2: HEK293 lysate (13 µg)
Lane 3: GPR55-transfected HEK293 lysate (13 µg)

•Also Available: **GPR55 Blocking Peptide** (10225)

Guanabenz (hydrochloride) 10851

Wytensin
MF: $C_8H_8Cl_2N_4$ • HCl **FW:** 267.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An α_2-adrenergic receptor agonist (effective concentrations 10-100 nM) with hypotensive effects; competes for imidazoline I_2-binding sites in brown adipose tissue (K_i = 97 nM)

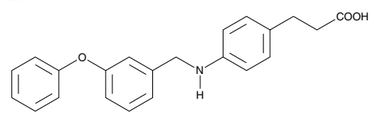
1 mg
5 mg
10 mg
50 mg



GW 9508 10008907

[885101-89-3]
MF: $C_{22}H_{21}NO_3$ **FW:** 347.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥1 year at -20°C
Summary: A small-molecule agonist of GPR40 (EC_{50} = 47 nM) and GPR120 (EC_{50} = 2.2 µM), GPCRs that are activated by medium and long-chain fatty acids; potentiates glucose-stimulated insulin secretion and the KCl-mediated increase in insulin secretion in MIN6 cells

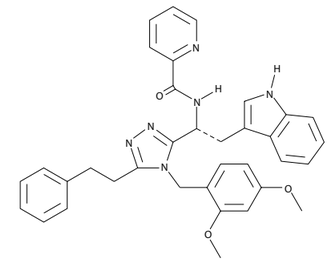
5 mg
10 mg
50 mg
100 mg



JMV3002 10012699

[925239-03-8]
MF: $C_{35}H_{34}N_6O_3$ **FW:** 586.7 **Purity:** ≥98%
A solution in methyl acetate **Stability:** ≥1 year at -20°C
Summary: A potent ghrelin receptor antagonist (IC_{50} = 1.1 nM) that inhibits hexarelin-stimulated food intake by as much as 98% in rats at 80 µg/kg; does not affect growth hormone release when tested in infant rats

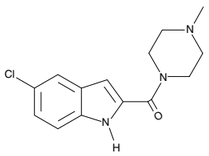
100 µg
500 µg
1 mg
5 mg



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

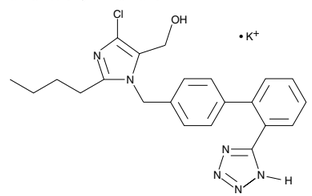
1 mg
5 mg
10 mg
50 mg



Losartan (potassium salt) 10006594

[124750-99-8] DuP 753, MK 954
MF: $C_{22}H_{23}ClN_6O$ • K **FW:** 461.0 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An AT_1 receptor antagonist (K_i = 5-20 nM); attenuates vein graft atherosclerosis in rabbits and reduces arterial blood pressure in rats; controls hypertension while protecting renal function, in humans

10 mg
50 mg
100 mg
500 mg



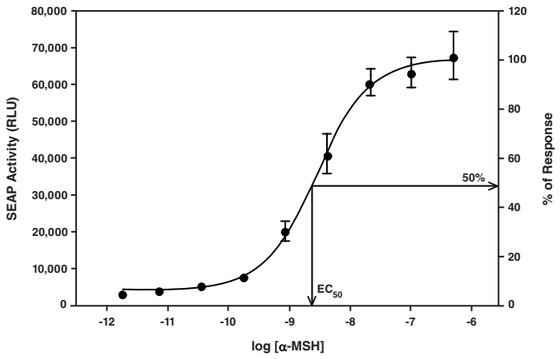
Melanocortin-3 Receptor STEP Reporter Assay Kit (Luminescence) 600180

MC3R

Stability: ≥1 year at -20°C

Summary: A cell-based screening assay based on novel transfection (STEP) technology

100 tests



Melanocortin-4 Receptor Polyclonal Antibody 10006355

MC4R

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

Summary: Antigen: mouse MC4R amino acids 21-33 • Host: rabbit • Cross Reactivity: (+) human, mouse, and rat MC4R • Application(s): IHC (formalin-fixed paraffin-embedded sections) and WB • MC4R receptor plays a critical role in appetite regulation and is a prime target for therapeutic intervention in obesity.

500 µl

•Also Available: **Melanocortin-4 Receptor Blocking Peptide** (10006356)

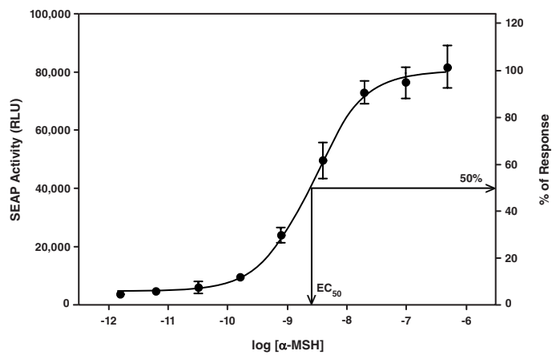
Melanocortin-4 Receptor STEP Reporter Assay Kit (Luminescence) 600190

MC4R

Stability: ≥1 year at -20°C

Summary: A cell-based screening assay based on novel transfection (STEP) technology

100 tests



(+)-Muscarine (iodide salt) 10230

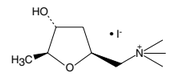
[24570-49-8]

MF: $C_9H_{20}NO_2$ • I **FW:** 301.2 **Purity:** ≥95%

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

Summary: A biologically active stereoisomer of muscarine that mimics the action of acetylcholine at muscarinic receptors

1 mg
5 mg
10 mg
25 mg



NO-Losartan A 10006456

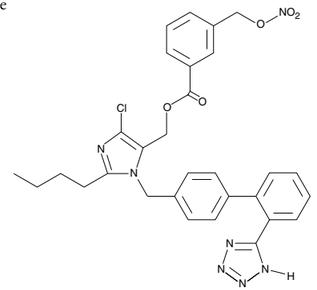
[791122-48-0]

MF: $C_{30}H_{28}ClN_7O_5$ **FW:** 602.0 **Purity:** ≥97%

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

Summary: A mammalian AT_1 receptor antagonist with a K_i value of 5-20 nM; in humans, losartan effectively controls hypertension while protecting renal function; possesses similar anti-hypertensive effects to losartan, with the addition of the vasodilating effects of NO release

1 mg
5 mg
10 mg
50 mg



NSC 23766 (hydrochloride) 13196

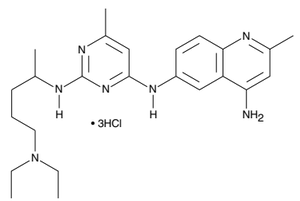
[1177865-17-6]

MF: $C_{24}H_{35}N_7$ • 3HCl **FW:** 531.0 **Purity:** ≥98%

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

Summary: A cell-permeable, reversible inhibitor of Rac1 activation by the Rac1-specific guanine nucleotide exchange factors TrioN and Tiam 1 (IC_{50} = 50 µM); has no effect on the closely related GTPases, Cdc42, and RhoA

1 mg
5 mg
10 mg
25 mg



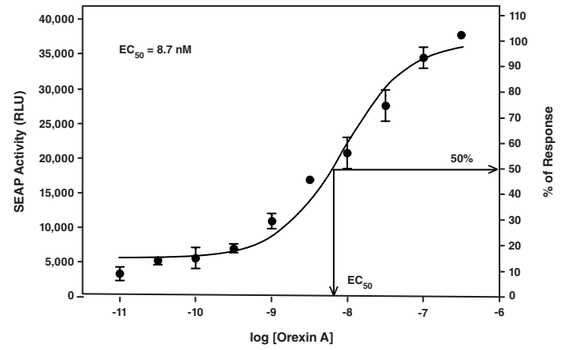
Orexin 1 Receptor STEP Reporter Assay Kit (Luminescence) 600240

OX1R

Stability: ≥1 year at -80°C

Summary: A cell-based screening assay based on novel transfection (STEP) technology

100 tests



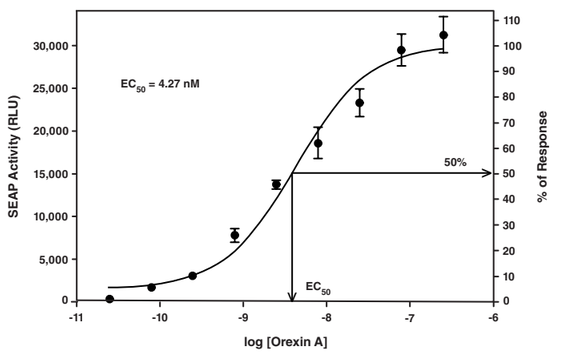
Orexin 2 Receptor STEP Reporter Assay Kit (Luminescence) 600250

OX2R

Stability: ≥1 year at -80°C

Summary: A cell-based screening assay based on novel transfection (STEP) technology

100 tests



PSN375963 10008593

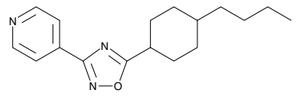
[388575-52-8]

MF: $C_{17}H_{23}N_3O$ **FW:** 285.4 **Purity:** ≥98%

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

Summary: A selective agonist of GPR119, a GPCR that mediates a reduction in food intake and body weight gain by oleoyl ethanolamide in rats; exhibits EC_{50} values of 8.4 and 7.9 µM at recombinant mouse and human GPR119 receptors, respectively

1 mg
5 mg
10 mg
25 mg



PSN632408 10008594

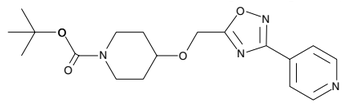
[857652-30-3]

MF: $C_{18}H_{24}N_4O_4$ **FW:** 360.4 **Purity:** ≥98%

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

Summary: A selective agonist of GPR119, a GPCR that mediates a reduction in food intake and body weight gain by oleoyl ethanolamide in rats; exhibits EC_{50} values of 5.6 and 7.9 µM at recombinant mouse and human GPR119 receptors, respectively

1 mg
5 mg
10 mg
25 mg



Purmorphamine 10009634

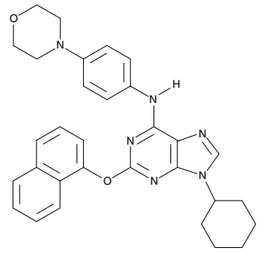
[483367-10-8]

MF: $C_{31}H_{32}N_6O_2$ **FW:** 520.6 **Purity:** ≥98%

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

Summary: A 2,6,9-trisubstituted purine that promotes the differentiation of both human and mouse mesenchymal progenitor cells into osteoblasts; binds to and activates the 7-transmembrane Smo receptor of the Hedgehog signaling pathway

1 mg
5 mg
10 mg
25 mg



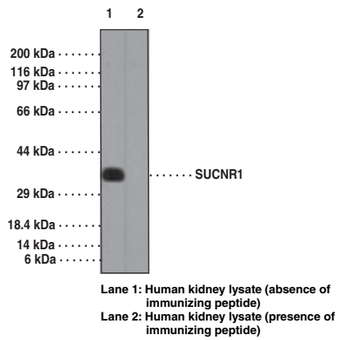
SUCNR1 Polyclonal Antibody 10928

GPR91

PBS **Stability:** ≥1 year at -20°C

Summary: Antigen: human SUCNR1 amino acids 100-150 • Host: rabbit • Cross Reactivity: (+) human, chimpanzee, new world monkey SUCNR1; predicted to react with dog, mouse, and rat SUCNR1 • Application(s): IHC and WB • SUCNR1 is a receptor for the citric acid cycle intermediate succinate that functions in establishing a neovascular network during development and in response to injury. It regulates the production of numerous angiogenic factors, including VEGF, and also is involved in the modulation of platelet function.

1 ea

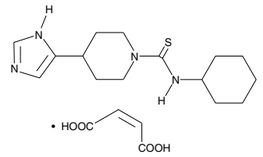


Lane 1: Human kidney lysate (absence of immunizing peptide)
Lane 2: Human kidney lysate (presence of immunizing peptide)

Thioperamide Maleate 10011127

[148440-81-7]
MF: $C_{15}H_{24}N_4S \bullet C_4H_4O_4$ **FW:** 408.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A selective histamine H_3 receptor antagonist that crosses the blood-brain barrier; binds to rat cerebral cortical cells *in vitro* with a pK_i value of 8.4

1 mg
5 mg
10 mg
25 mg



Lipid Neurotransmitters

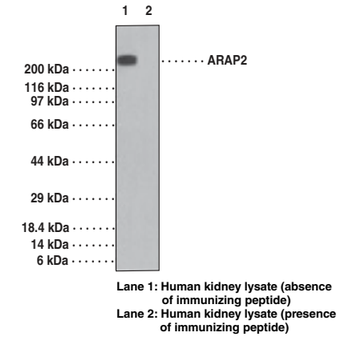
Item No.	Product Name	Summary
62160	2-Arachidonoyl Glycerol	Endogenous CB_1 (K_i = 58 nM) and CB_2 (K_i = 145nM) receptor agonist
62165	2-Arachidonyl Glycerol ether	Selective CB_1 receptor agonist exhibiting K_i values of 21.2 nM and >3 µM at the CB_1 and CB_2 receptors, respectively; more chemically stable than 2-AG, with an endogenous half-life of hours rather than minutes
90054	Arachidonoyl 2'-Fluoroethylamide	Selective CB_1 receptor agonist with K_i values of 26.7 nM and 908 nM for the CB_1 and CB_2 receptors, respectively; remains a good FAAH substrate
13261	URB447	A mixed central cannabinoid (CB_1) receptor antagonist/peripheral cannabinoid (CB_2) receptor agonist with IC_{50} values of 313 and 41 nM, respectively; does not penetrate the blood brain barrier as observed with Rimonabant
9000484	Rimonabant	Widely used as a tool to investigate CB receptor properties and the mechanisms by which CB agonists exert their pharmacological effects
90050	Arachidonoyl Ethanolamide	Endogenous CB_1 (K_i = 52 nM) and CB_2 (K_i = 1930 nM) receptor agonist
70275	IMMA	Selective CB_2 receptor agonist; binding constant for the CB_2 receptor is 435 nM compared to >20,000 nM for the CB_1 receptor
90055	(±)-2-Methyl Arachidonoyl-2'-fluoroethylamide	Potent CB_1 receptor agonist with a K_i value of 5.7 nM (rat brain)
10009280	L-759,633	A high-affinity CB_2-selective receptor agonist with K_i values of 6.4 and 1,043 nM for CB_2 and CB_1 receptors, respectively; inhibits forskolin-stimulated cyclic AMP production in CHO cells transfected with CB_2 or CB_1 receptors with IC_{50} values of 8.1 nM and 10 µM, respectively
13058	N-Oleoyl-L-Serine	An endogenous lipid that has been reported to stimulate bone formation and to inhibit bone resorption
10008642	oxy-Arachidonoyl Ethanolamide	A selective ligand for the CB_2 receptor with K_i values of 0.47 and 0.081 µM for human CB_1 and human CB_2, respectively; first known fatty acid amide with a reversed CB_1/CB_2 affinity ratio
90052	Arvanil	Has complex interactions with the cannabinoid system; potentiates the agonist activity of endogenous cannabinoids by inhibiting the reuptake of AEA; is an agonist at CB_1 (K_i values of 0.25-0.52 µM), but not CB_2, receptors; resistant to hydrolysis by FAAH
90262	Olvanil	A structural analog of capsaicin, which is the noxious active component of hot peppers of the Capsicum family; acts as an agonist at the vanilloid receptor, VR1, inducing desensitization analgesia in rat and murine models of pain; a CB_1 agonist, but does not bind to CB_2 receptors or inhibit fatty acid amide hydrolase
10010372	GW 842166X	A potent CB_2 receptor agonist with ED_{50} values of 91 and 63 nM in rat and human, respectively
10004259	CAY10429	Abnormal cannabidiol; a synthetic regioisomer of cannabidiol that fails to elicit either CB_1 or CB_2 responsiveness and is without psychotropic activity; believed to activate a third type of CB receptor, provisionally called the non-CB_1/CB_2 endocannabinoid receptor
10004184	NESS 0327	An extremely potent CB receptor antagonist with high selectivity for the central CB_1 receptor (K_i = 0.35 pM) compared to the peripheral CB_2 receptor (K_i = 21 nM); competitively inhibits the binding of WIN 55,212-2 in isolated rat cerebella membranes and mouse vas deferens; does not act as an inverse agonist and does not produce any physiological effects of its own
10009195	O-2545 (hydrochloride)	A potent water-soluble CB_1 and CB_2 receptor agonist with K_i values of 1.5 and 0.32 nM, respectively
10009022	(S)-SLV 319	A potent and selective CB_1 receptor antagonist with K_i values of 7.8 and 7,943 nM for CB_1 and CB_2, respectively; less lipophilic (log P = 5.1) and therefore more water soluble than other CB_1 receptor ligands **Also Available: (R)-SLV 319 (10009227), (±)-SLV 319 (10009226)**
91054	Arachidonoyl 2'-Chloroethylamide	Potent, stable, and selective CB_1 receptor agonist with K_i values of 1.4 nM and 3.1 µM at the isolated rat CB_1 and CB_2 receptors, respectively **Also Available: Arachidonoyl Cyclopropylamide (91053)**
10008669	CAY10508	A potent and selective CB_1 receptor inverse agonist with a K_i value of 243 nM and an EC_{50} value of 195 nM; a concentration of 10 µM resulted in 100% and 35% displacement of [3H]-CP-55,940 at the CB_1 and CB_2 receptors, respectively
10010398	CB13	A dual agonist of the CB_1 (IC_{50} = 15 nM) and CB_2 (IC_{50} = 98 nM) receptors

Phospholipid/Sphingolipid Signaling

ARAP2 Polyclonal Antibody 13495

Centaurin-δ-1
Protein A-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human ARAP2 within the region of amino acids 1,670-1,720 • Host: rabbit • Cross Reactivity: (+) human ARAP2 • Application(s): IHC and WB • ARAP2 is a PIP3-dependent GTPase-activating protein that binds to RhoA-GTP, and modulates actin cytoskeleton remodeling by regulating ARF and RHO family members. ARAP2 associates with focal adhesions and functions downstream of RhoA to regulate focal adhesion dynamics.

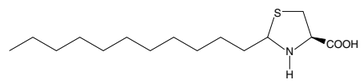
1 ea



CAY10444 10005033

[298186-80-8] BML-241
MF: $C_{15}H_{29}NO_2S$ **FW:** 287.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥1 year at -20°C
Summary: A selective antagonist of S1P binding to the $S1P_3$ receptor; blocks calcium increase in HeLa cells by about 40% at 10 µM

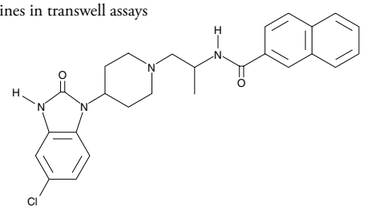
5 mg
10 mg
25 mg
50 mg



CAY10593 13206

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

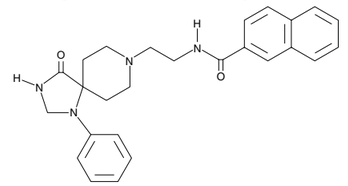
1 mg
5 mg
10 mg
25 mg



CAY10594 13207

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

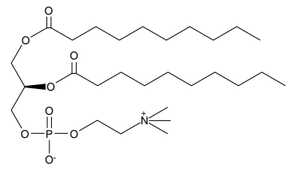
1 mg
5 mg
10 mg
25 mg



1,2-Didecanoyl PC 10009879

[3436-44-0] Didecanoyl Lecithin, 1,2-Didecanoyl Phosphatidylcholine
MF: $C_{28}H_{56}NO_8P$ **FW:** 565.7 **Purity:** ≥98%
A solution in ethanol **Stability:** ≥1 year at -20°C
Summary: A synthetic, less hydrophobic phospholipid that has been found to be useful for enhancing the absorption of peptide drugs and hormones such as insulin

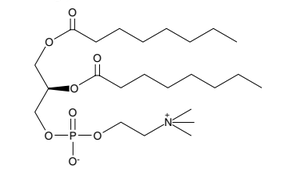
5 mg
10 mg
25 mg
50 mg



1,2-Dioctanoyl PC 10009874

[19191-91-4] 1,2-Dioctanoyl Phosphatidylcholine
MF: $C_{24}H_{48}NO_8P$ **FW:** 509.6 **Purity:** ≥98%
A solution in ethanol **Stability:** ≥1 year at -20°C
Summary: A synthetic analog of natural PC species containing saturated C8:O fatty acids in the *sn*-1 and *sn*-2 positions of the glycerol backbone

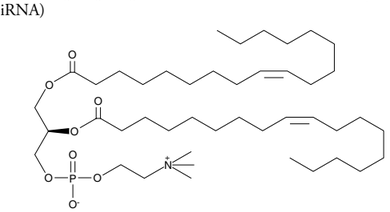
5 mg
10 mg
25 mg
50 mg



1,2-Dioleoyl PC 10009873

[56648-95-4] 1,2-dioleoyl-sn-glycero-3-Phosphatidylcholine, DOPC
MF: $C_{44}H_{84}NO_8P$ **FW:** 786.2 **Purity:** ≥98%
A solution in ethanol **Stability:** ≥1 year at -20°C
Summary: A dimonounsaturated phospholipid used for efficient *in vivo* delivery of short interfering RNA (siRNA)

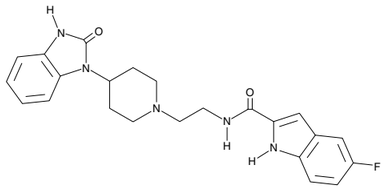
10 mg
25 mg
50 mg
100 mg



FIPI 13563

[939055-18-2] 5-Fluoro-2-Indolyl des-Chlorohalopemide
MF: $C_{23}H_{24}FN_5O_2$ **FW:** 421.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A derivative of halopemide which potently inhibits both PLD_1 (IC_{50} = 25 nM) and PLD_2 (IC_{50} = 20 nM); prevents PLD regulation of F-actin cytoskeleton reorganization, cell spreading, and chemotaxis

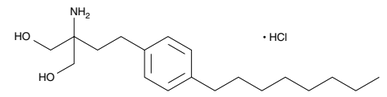
1 mg
5 mg
10 mg
25 mg



FTY720 10006292

[162359-56-0]
MF: $C_{19}H_{33}NO_2$ • HCl **FW:** 343.9 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A structural analog of sphingosine and a novel immune modulator; inhibits lymphocyte emigration from lymphoid organs; becomes phosphorylated by sphingosine kinase *in vivo* to act as a potent agonist at $S1P_1$, $S1P_3$, $S1P_4$, and $S1P_5$

5 mg
10 mg
25 mg
50 mg

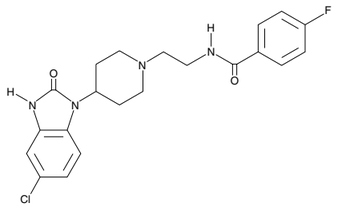


•Also Available: **FTY720 phenoxy-biotin** (13254)
NBD-FTY720 phenoxy (hydrochloride) (16841)
FTY720 Phosphate (10008639)
FTY720 (R)-Phosphate (10006407)
FTY720 (S)-Phosphate (10006408)
azido-FTY720 (10008612)

Halopemide 13205

[59831-65-1] NSC 354856, R34301
MF: $C_{21}H_{22}ClFN_4O_2$ **FW:** 416.2 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent inhibitor of PLD, inhibiting human PLD_1 and PLD_2 *in vitro* (IC_{50} = 220 and 310 nM, respectively) and PLD activity in cells; inhibits the dopamine receptor

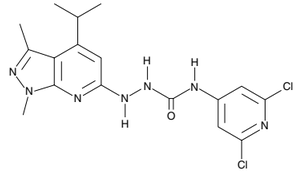
1 mg
5 mg
10 mg
25 mg



JTE-013 10009458

[383150-41-2]
MF: $C_{17}H_{19}Cl_2N_7O$ **FW:** 408.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent, selective $S1P_2$ receptor antagonist that binds to the human and rat receptors with IC_{50} values of 17 and 22 nM, respectively

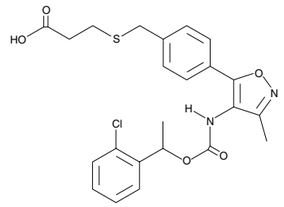
1 mg
5 mg
10 mg
50 mg



Ki16425 10012659

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

1 mg
5 mg
10 mg
100 mg



LPA_1 Polyclonal Antibody 10005280

EDG-2, $LPAR_1$, LPA Receptor 1, Vzg-1
Peptide affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human lysophosphatidic acid 1 (LPA_1) amino acids 342-359 • Host: rabbit • Cross Reactivity: (+) bovine, human, mouse, ovine, and rat LPA_1 • Application(s): ICC and WB • LPA_1 is a GPCR that couples with three types of G proteins, $G_{i/o}$, G_q, and $G_{12/13}$ to induce a range of cellular responses including activation of phospholipase C, multiple kinases, the serum response element and cell proliferation.

500 µl

•Also Available: **LPA_1 Blocking Peptide** (10006984)

LPA_3 Polyclonal Antibody 10004840

EDG-7, LPAR3
Peptide affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: mouse LPA_3 N-terminal amino acids 1-12 • Host: rabbit • Cross Reactivity: (+) human, mouse, and rat LPA_3 • Application(s): ICC and WB • LPA_3 is a GPCR that mediates many cellular responses including cytoskeletal rearrangements, cell proliferation, and inhibition of gap junction communication.

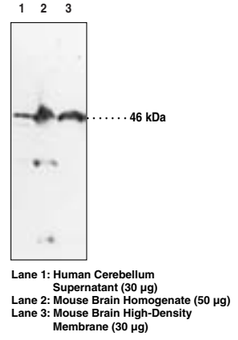
500 µl

•Also Available: **LPA_3 Blocking Peptide** (10005092)

NAPE-PLD Polyclonal Antibody (aa 6-20) 10306

N-Acyl-Phosphatidylethanolamine-Hydrolysing Phospholipase D
Affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human NAPE-PLD amino acids 6-20 • Host: rabbit • Cross Reactivity: (+) human, mouse, rat, and bovine NAPE-PLD • Application(s): WB • NAPE-PLD catalyzes the hydrolysis of NAPE to form N-acylethanolamines (NAEs), which are involved in diverse biological processes such as inflammatory regulation, apoptosis, and tissue degeneration.

500 µl



Lane 1: Human Cerebellum Supernatant (30 µg)
Lane 2: Mouse Brain Homogenate (50 µg)
Lane 3: Mouse Brain High-Density Membrane (30 µg)

•Also Available: **NAPE-PLD Blocking Peptide (aa 6-20)** (10304)

NAPE-PLD Polyclonal Antibody (aa 159-172) 10305

N-Acyl-Phosphatidylethanolamine-Hydrolysing Phospholipase D
Affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human NAPE-PLD amino acids 159-172 • Host: rabbit • Cross Reactivity: (+) human, mouse, and rat NAPE-PLD • Application(s): WB • NAPE-PLD catalyzes the hydrolysis of NAPE to form N-acylethanolamines (NAEs), which are involved in diverse biological processes such as inflammatory regulation, apoptosis, and tissue degeneration.

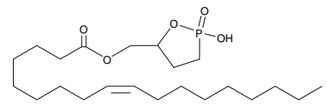
500 µl

•Also Available: **NAPE-PLD Blocking Peptide (aa 159-172)** (10303)

Oleoyl 3-carbacyclic Phosphatidic Acid 10010299

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

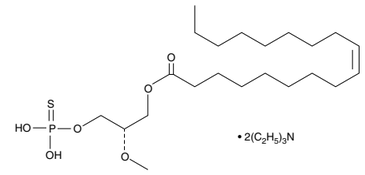
500 µg
1 mg
5 mg
10 mg



(2S)-OMPT 10005707

MF: $C_{22}H_{43}O_6PS$ • $2(C_2H_5)_3N$ **FW:** 655.0 **Purity:** ≥98%
A solution in ethanol:chloroform (1:1) **Stability:** ≥1 year at -20°C
Summary: A selective agonist of the LPA_3 receptor; exhibits EC_{50} values of 68 nM and > 6.8 µM for the calcium mobilization in LPA_3 and LPA_2-expressing *Sf*9 cells, respectively

500 µg
1 mg
5 mg
10 mg



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

Protein-A purified IgG_{2a} **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, polymorphonuclear leukocytes, monocytes, and macrophages. PAF increases vascular permeability, decreases cardiac output, induces hypotension, and stimulates uterine contraction.

1 ea

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

PAF Receptor (human) Polyclonal Antibody 160602

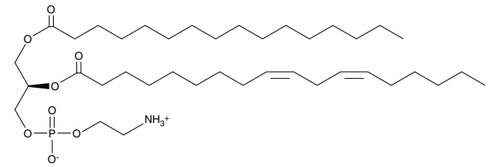
Peptide affinity-purified IgG **Stability:** ≥1 year at-20°C
Summary: Antigen: human PAF receptor amino acids 1-17 • Host: rabbit • Cross Reactivity: (+) human, mouse, rat, and porcine PAF receptors • Application(s): FC, ICC, and WB • PAF is a biologically active phospholipid whose biological effects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

500 µl

1-Palmitoyl-2-linoleoyl PE 10007072

[26662-95-3] Phosphatidyl Ethanolamine (1-palmitoyl, 2-linoleoyl), PLPE
MF: $C_{39}H_{74}NO_8P$ **FW:** 716.0 **Purity:** ≥98%
A solution in chloroform **Stability:** ≥6 months at -20°C
Summary: One of the many phosphatidylethanolamines that may be present in cellular membranes

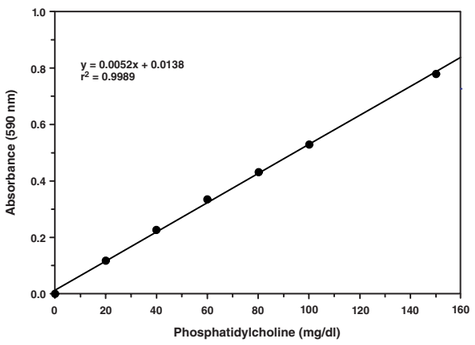
5 mg
10 mg
50 mg
100 mg



Phosphatidylcholine Assay Kit 10009926

PC
Stability: ≥1 year at -20°C
Summary: A colorimetric assay for the quantification of phosphatidylcholine in plasma or serum

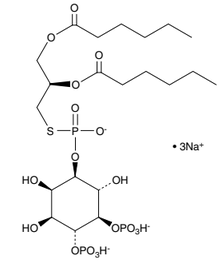
96 wells



PLC thio-PIP_2 (sodium salt) 10007839

MF: $C_{21}H_{38}O_{18}P_3S$ • 3Na **FW:** 772.5 **Purity:** ≥98%
A lyophilized powder **Stability:** ≥1 year at -20°C
Summary: An analog of PIP_2 that contains sulfur rather than oxygen at the *sn*-3 position of the glycerol backbone; can be used in conjuction with Ellman's reagent to allow colorimetric quantitation of PLC activity

100 µg
500 µg
1 mg
5 mg



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

GRP1 PH Domain, PI(3,4,5)-P_3, PIP_3
M_r: ~41.7 kDa **Purity:** ≥95%
Source: Recombinant N-terminal GST-tagged protein purified from *E. coli*

25 µg
50 µg
100 µg

PtdIns-(4)-P_1 Binding Protein 10009241

PI(4)-P_1, PIP, SidC, $SidC_3C$
M_r: ~132 kDa (GST-tagged), 106 kDa (native) **Purity:** ≥90%
Source: Recombinant N-terminal GST-tagged protein purified from *E. coli*

25 µg
50 µg
100 µg

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

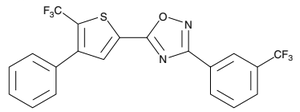
PI(4,5)-P_2, PIP_2, PLC-δ1-PH Domain
M_r: ~45.2 kDa **Purity:** ≥95%
Source: Recombinant N-terminal GST-tagged protein purified from *E. coli*

25 µg
50 µg
100 µg

SEW2871 10006440

[256414-75-2]
MF: $C_{20}H_{10}F_6N_2OS$ **FW:** 440.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A selective $S1P_1$ receptor agonist in both human and mouse

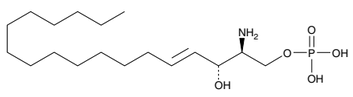
5 mg
10 mg
25 mg
50 mg



Shingosine-1-Phosphate 62570

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

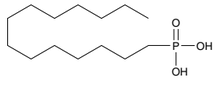
1 mg
5 mg
10 mg
25 mg



Tetradecyl Phosphonate 10007565

[4671-77-4]
MF: $C_{14}H_{31}O_3P$ **FW:** 278.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A pan-antagonist of LPA_{1-3} receptors (IC_{50} = 10, 5.5, and 3.1 µM, respectively)

100 mg
500 mg
1 g
5 g



$S1P_1$ Polyclonal Antibody 10005228

EDG-1, S1PR1
Peptide affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human $S1P_1$ amino acids 241-253 • Host: rabbit • Cross Reactivity: (+) human, mouse, porcine, and rat $S1P_1$ • Application(s): ICC, IHC (paraffin-embedded sections), and WB • S1P exerts its activity by binding to five distinct GPCRs, $S1P_1$/EDG-1, $S1P_2$/EDG-5, $S1P_3$/EDG-3, $S1P_4$/EDG-6, and $S1P_5$/EDG-8. $S1P_1$ primarily mediates S1P-induced cell proliferation, survival, migration, cytoskeletal organization, and morphogenesis. Expression of $S1P_1$ is abundant in embryological vasculature and is ubiquitously expressed in adult cells suggesting diverse physiological functions of this receptor.

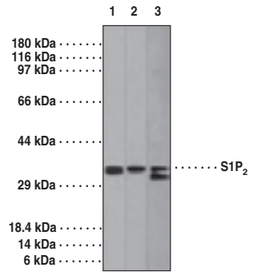
500 µl
Trial Size

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

$S1P_2$ Polyclonal Antibody 13488

EDG-5, S1PR2
Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: synthetic peptide from human $S1P_2$ amino acids 325-343 • Host: rabbit • Cross Reactivity: (+) human, monkey, mouse, and rat $S1P_2$ • Application(s): WB • $S1P_2$ acts as a receptor for the bioactive lipid S1P and participates in S1P-induced cell proliferation, survival, and transcriptional activation.

1 ea

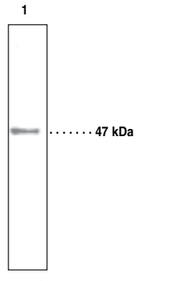


Lane 1: Human heart lysate
Lane 2: Mouse heart lysate
Lane 3: Rat heart lysate

$S1P_3$ Polyclonal Antibody 10006373

EDG-3, S1PR3
Peptide affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human $S1P_3$ amino acids 12-25 • Host: rabbit • Cross Reactivity: (+) human, mouse, and rat $S1P_3$ • Application(s): ICC and WB • $S1P_3$ is one of five GPCRs that are activated by S1P. It couples to $G_{i/o}$-ERK, G_q-PLC, and $G_{12/13}$-Rho axes to mediate S1P-induced cell proliferation, survival, migration, and related signaling events. $S1P_3$ is widely expressed in various tissues, suggesting diverse physiological functions of this receptor.

500 µl



Lane 1: Human cerebral cortex membrane (30 µg)

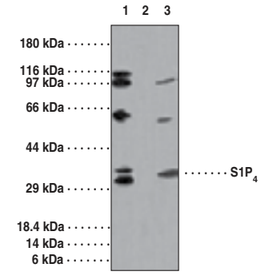
DAGs

Item No.	Product Name
9000341	1-NBD-decanoyl-2-decanoyl-*sn*-Glycerol
62210	1,2-Didecanoyl-*sn*-glycerol
10008646	1,2-Dihexanoyl-*sn*-glycerol
10007863	1,2-Dioleoyl-*rac*-glycerol
62225	1,2-Dioctanoyl-*sn*-glycerol
62230	1,2-Dioleoyl-*sn*-glycerol
10008648	1,2-Dipalmitoyl-*sn*-glycerol
60920	Hexadecyl Acetyl Glycerol
60930	Hexadecyl Methyl Glycerol
62600	1-Oleoyl-2-acetyl-*sn*-glycerol
10008650	1-Stearoyl-2-Arachidonoyl-*sn*-Glycerol
10009864	1-Stearoyl-2-Arachidonoyl PC
10011300	NBD-Stearoyl-2-Arachidonoyl-*sn*-glycerol

$S1P_4$ Polyclonal Antibody 13489

EDG-6, S1PR4
Peptide affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: synthetic peptide from human $S1P_4$ wihin the region of amino acids 1-50 • Host: rabbit • Cross Reactivity: (+) human and mouse $S1P_4$ • Application(s): ICC, IF, and WB • Binding of S1P to $S1P_4$ activates Erk, leading to the activation of the transcription factor Elk1 and thus the MAPK signal transduction pathway.

1 ea



Lane 1: Jurkat cell lysate
Lane 2: Jurkat cell lysate (antibody blocked with immunizing peptide)
Lane 3: RAW cell lysate

Lysophosphatidic Acid and Sphingosine-1-Phosphate Receptor Ligands

Item No.	Product Name	Activity	Receptor Target	Effective Concentration
10006292	FTY720	Agonist	$S1P_{1,3,4,5}$	
10009458	JTE-013	Antagonist	$S1P_2$	IC_{50} = 17 nM human; 22 nM rat
10012659	Ki16425	Antagonist	LPA_1 LPA_2 LPA_3	K_i = 0.34 µM K_i = 6.5 µM K_i = 0.93 µM
10010299	Oleoyl 3-carbacyclic Phosphatidic Acid	Antagonist	LPA_1 LPA_3	IC_{50} = 836 nM IC_{50} = 440 nM
10005707	(2S)-OMPT	Agonist	LPA_3	EC_{50} = 68 nM
10006440	SEW2871	Agonist	$S1P_1$	
62570	Sphingosine-1-Phosphate			
10007565	Tetradecyl Phosphonate	Antagonist	LPA_1 LPA_2 LPA_3	IC_{50} = 10 µM IC_{50} = 5.5 µM IC_{50} = 3.1 µM
10010992	W123	Antagonist	$S1P_1$	K_i = 0.69 µM
10009109	W146 (trifluoroacetate salt)	Antagonist	$S1P_1$	K_i = 77 nM

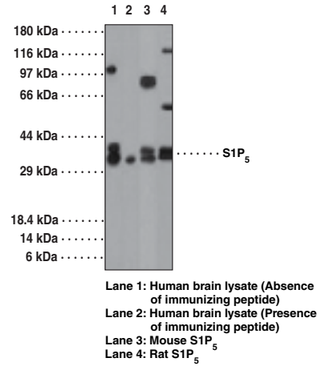
$S1P_5$ Polyclonal Antibody 13490

EDG-8, S1PR5

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

Summary: Antigen: peptide from human $S1P_5$ within the region of amino acids 1-50 • Host: rabbit • Cross Reactivity: (+) canine, human, monkey, mouse, and rat $S1P_5$ • Application(s): IHC and WB • $S1P_5$ is a receptor for the bioactive sphingolipid S1P as well as for LPA and gives diverse physiological effects on most types of cells and tissues.

1 ea



1-Stearoyl-2-Arachidonoyl PC 10009864

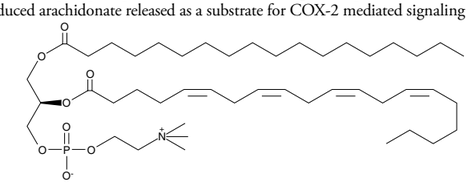
[35418-59-8] SAPC, 1-Stearoyl-2-Arachidonoyl Phosphatidylcholine

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 the $cPLA_2$; an important source of activation-induced arachidonate released as a substrate for COX-2 mediated signaling

1 mg
5 mg
10 mg
25 mg



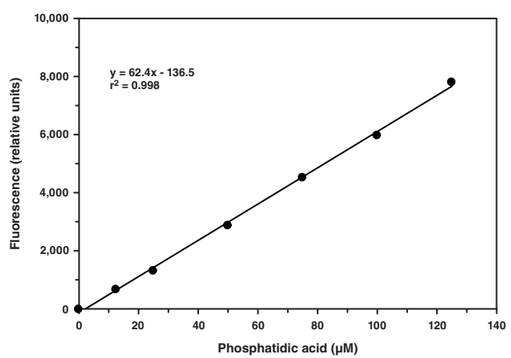
Total Phosphatidic Acid Assay Kit 700240

PA

Stability: ≥1 year at -20°C

Summary: A fluorescence-based method for detecting phosphatidic acid in crude cultured cellular lipids

96 wells



(±)*trans*-2,5-*bis*-(3,4,5-Trimethoxyphenyl)-1,3-dioxolane 60950

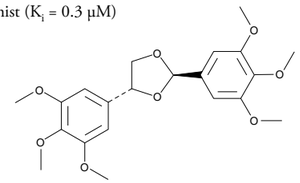
[116673-45-1] trans-BTP Dioxolane

MF: $C_{21}H_{26}O_8$ **FW:** 406.4 **Purity:** ≥98%

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

Summary: A PAF receptor antagonist (K_i = 0.3 µM)

1 mg
5 mg
10 mg
50 mg



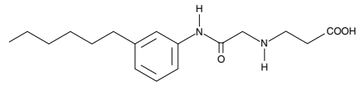
W123 10010992

MF: $C_{17}H_{26}N_2O_3$ **FW:** 306.4 **Purity:** ≥98%

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

Summary: An analog of FTY720 that is a competitive antagonist of $S1P_1$; has a K_i value of 0.69 µM when assessed by SEW2871-induced activation of $S1P_1$

1 mg
5 mg
10 mg
25 mg



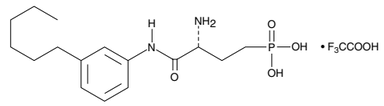
W146 (trifluoroacetate salt) 10009109

MF: $C_{16}H_{27}N_2O_4P \bullet C_2HF_3O_2$ **FW:** 456.4 **Purity:** ≥95%

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

Summary: A potent, selective $S1P_1$ receptor antagonist that exhibits a K_i value of 77 nM for the human receptor with no activity at 10 µM at $S1P_2$, $S1P_3$, or $S1P_5$ receptors; causes capillary leakage and inhibition of $S1P_1$ agonist-induced lymphocyte sequestration *in vivo*

500 µg
1 mg
5 mg
10 mg



YM-201636 13576

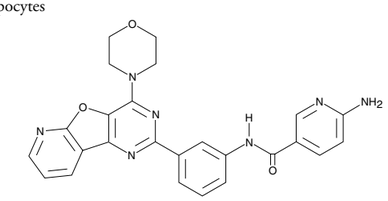
[371942-69-7]

MF: $C_{25}H_{21}N_7O_3$ **FW:** 467.5 **Purity:** ≥95%

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

Summary: A cell-permeable and selective inhibitor of PIKfyve (IC_{50} = 33 nM); reversibly impairs endosomal trafficking in NIH3T3 cells and blocks retroviral exit by budding from cells; inhibits basal and insulin-activated 2-deoxyglucose uptake (IC_{50} = 54 nM) in adipocytes

1 mg
5 mg
10 mg
25 mg



Inositol Phospholipids

Item No.	Product Name
10009879	1,2-Didecanoyl PC
10009874	1,2-Dioctanoyl PC
10009873	1,2-Dioleoyl PC
10007072	1-Palmitoyl-2-linoleoyl PE
10007839	PLC thio-PIP2 (sodium salt)
10009804	3-PT-PtdIns-(3,4,5)-P_3 (1,2-dioctanoyl) (sodium salt)
10010181	Ptd(S)Ins-(3,4)-P_2 (1,2-dioctanoyl) (sodium salt)
10010112	Ptd(S)Ins-(3,4)-P_2 (1,2-dipalmitoyl) (sodium salt)
9000660	PtdIns-(1,2-dihexanoyl) (sodium salt)
10008099	PtdIns-(1,2-dioctanoyl) (sodium salt)
10007710	PtdIns-(1,2-dipalmitoyl) (ammonium salt)
9000305	PtdIns-(1-arachidonoyl, 2-arachidonoyl-d_8) (ammonium salt)
9000304	PtdIns-(1-arachidonoyl-d_8, 2-arachidonoyl) (sodium salt)
10008394	PtdIns-(3)-P_1 (1,2-dioctanoyl) (sodium salt)
64921	PtdIns-(3)-P_1 (1,2-dipalmitoyl) (ammonium salt)
10005616	PtdIns-(3)-P_1 (1,2-dipalmitoyl)-d_{62} (ammonium salt)
10007759	PtdIns-(3,4)-P_2 (1,2-dihexanoyl) (sodium salt)
10008400	PtdIns-(3,4)-P_2 (1,2-dioctanoyl) (sodium salt)
64922	PtdIns-(3,4)-P_2 (1,2-dipalmitoyl) (sodium salt)
10008390	PtdIns-(3,4,5)-P_3 (1,2-dihexanoyl) (ammonium salt)
10007764	PtdIns-(3,4,5)-P_3 (1,2-dioctanoyl) (sodium salt)
9000414	PtdIns-(3,4,5)-P_3 (1,2-dipalmitoyl) (sodium salt)
64930	PtdIns-(3,4,5)-P_3 (1-stearoyl, 2-arachidonoyl) (sodium salt)
9000829	PtdIns-(3,4,5)-P_3 (1-stearoyl, 2-docosahexaenoyl) (sodium salt)
10010383	PtdIns-(3,4,5)-P_3-fluorescein (ammonium salt)
10009531	PtdIns-(3,4,5)-P_3-biotin (sodium salt)
10008396	PtdIns-(3,5)-P_2 (1,2-dihexanoyl) (sodium salt)
10007763	PtdIns-(3,5)-P_2 (1,2-dioctanoyl) (sodium salt)
10008398	PtdIns-(3,5)-P_2 (1,2-dipalmitoyl) (sodium salt)
10007757	PtdIns-(4)-P_1 (1,2-dihexanoyl) (sodium salt)
10007711	PtdIns-(4)-P_1 (1,2-dioctanoyl) (ammonium salt)
9000656	PtdIns-(4)-P_1 (1,2-dioctanoyl)-biotin (sodium salt)
64923	PtdIns-(4)-P_1 (1,2-dipalmitoyl) (ammonium salt)
9000655	PtdIns-(4)-P_1-fluorescein (ammonium salt)
10007762	PtdIns-(4,5)-P_2 (1,2-dihexanoyl) (sodium salt)
64910	PtdIns-(4,5)-P_2 (1,2-dioctanoyl) (sodium salt)
64924	PtdIns-(4,5)-P_2 (1,2-dipalmitoyl) (ammonium salt)
10008115	PtdIns-(4,5)-P_2 (1,2-dipalmitoyl) (sodium salt)
10005615	PtdIns-(4,5)-P_2 (1,2-dipamitoyl)-d_{62} (sodium salt)
10008159	PtdIns-(4,5)-P_2-biotin (sodium salt)
10010388	PtdIns-(4,5)-P_2-fluorescein (ammonium salt)
10008050	PtdIns-(5)-P_1 (1,2-dihexanoyl) (sodium salt)
10007758	PtdIns-(5)-P_1 (1,2-dioctanoyl) (ammonium salt)
64925	PtdIns-(5)-P_1 (1,2-dipalmitoyl) (ammonium salt)

Item No.	Product Name
10009864	1-Stearoyl-2-Arachidonoyl PC
10008448	D-*myo*-Inositol-1,2,3,4-tetraphosphate (sodium salt)
10008453	D-*myo*-Inositol-1,2,3,5,6-pentaphosphate (sodium salt)
10008449	D-*myo*-Inositol-1,2,3,5-tetraphosphate (sodium salt)
10008450	D-*myo*-Inositol-1,2,3,6-tetraphosphate (sodium salt)
10008452	D-*myo*-Inositol-1,2,4,5,6-pentaphosphate (sodium salt)
10008451	D-*myo*-Inositol-1,2,4,5-tetraphosphate (sodium salt)
10008444	D-*myo*-Inositol-1,2,5,6-tetraphosphate (sodium salt)
10007780	D-*myo*-Inositol-1,2,6-triphosphate (sodium salt)
10008439	D-*myo*-Inositol-1,2-diphosphate (sodium salt)
10009851	D-*myo*-Inositol-1,3,4,5,6-pentaphosphate (ammonium salt)
10007784	D-*myo*-Inositol-1,3,4,5,6-pentaphosphate (sodium salt)
60980	D-*myo*-Inositol-1,3,4,5-tetraphosphate (sodium salt)
10008442	D-*myo*-Inositol-1,3,4,6-tetraphosphate (ammonium salt)
60972	D-*myo*-Inositol-1,3,4-triphosphate (sodium salt)
10007781	D-*myo*-Inositol-1,3,5-triphosphate (sodium salt)
10008443	D-*myo*-Inositol-1,3-diphosphate (sodium salt)
10007783	D-*myo*-Inositol-1,4,5,6-tetraphosphate (sodium salt)
60960	D-*myo*-Inositol-1,4,5-triphosphate (potassium salt)
10008205	D-*myo*-Inositol-1,4,5-triphosphate (sodium salt)
10008427	D-*myo*-Inositol-1,4,6-triphosphate (sodium salt)
10008438	D-*myo*-Inositol-1,4-diphosphate (sodium salt)
10008422	D-*myo*-Inositol-1,5,6-triphosphate (sodium salt)
10008441	D-*myo*-Inositol-1,5-diphosphate (sodium salt)
10007777	D-*myo*-Inositol-1-phosphate (sodium salt)
10008456	D-*myo*-Inositol-2,3,4,5-tetraphosphate (ammonium salt)
10008455	D-*myo*-Inositol-2,3,5,6-tetraphosphate (sodium salt)
10008423	D-*myo*-Inositol-2,3,5-triphosphate (ammonium salt)
10007779	D-*myo*-Inositol-2,4,5-triphosphate (sodium salt)
10008419	D-*myo*-Inositol-2,4-diphosphate (sodium salt)
10008424	D-*myo*-inositol-2,5,6-triphosphate (sodium salt)
10007782	D-*myo*-Inositol-3,4,5,6-tetraphosphate (sodium salt)
10008425	D-*myo*-Inositol-3,4,5-triphosphate (sodium salt)
10007778	D-*myo*-Inositol-3-phosphate (sodium salt)
10008418	D-*myo*-Inositol-4,5-diphosphate (sodium salt)
10008437	D-*myo*-Inositol-4-phosphate (ammonium salt)
10008426	L-*myo*-Inositol-1,4,5-triphosphate (sodium salt)

Inositol Phospholipid Related Recombinant Proteins

Item No.	Product Name
10009241	PtdIns-(4)-P_1 Binding Protein
10009815	PtdIns-(4,5)-P_2 Binding Protein
10009817	PtdIns-(3,4,5)-P_3 Binding Protein
10009746	PTEN (human recombinant)

Olivia L. May, Ph.D.

Toll-like Receptors: Immune Signaling Sentinels

Toll-like receptors (TLRs) are important innate immune proteins responsible for the identification and clearance of invading pathogens. They are pattern recognition receptors (PRRs) capable of recognizing specific pathogen-associated molecular patterns (PAMPs) conserved among micro-organisms and also recognize damage-associated molecular patterns (DAMPs) from tissue injury or cell death resulting from inflammation, oxidative stress, necrosis, etc. Ultimately, TLRs act as sentinels, providing an immediate first line of defense against invading microbes leading to the activation of defense mechanisms of the innate immune system. They are also important for developing B and T cell-mediated, pathogen-specific adaptive immune "memories".

That's Weird!

Curious about the name? These receptors were named for their similarity to the protein coded by the Toll gene identified in *Drosophila* in the mid 80s by Christiane Nüsslein-Volhard and Eric Wieschaus, developmental biologists at the Max Planck Institute.[1] The gene in question, when mutated, makes *Drosophila* embryos develop ventrally, when in normal development this should occur dorsally. As the story goes, the two researchers were so surprised when first viewing this unusual mutation from opposite sides of a double microscope that they both spontaneously looked up at one another and exclaimed "Das ist ja toll!", or "That's weird!". As it turns out, the toll gene is not only important for embryonic polarity during *Drosophila* development (a Nobel prize-winning discovery), but plays a key role in mammalian innate and adaptive immunity.

Ligands

Most mammals have 10 to 13 different TLRs (10 functional TLRs have been identified in humans) that specialize in identifying the molecular fingerprints of invading pathogens to activate an appropriate immune signaling pathway tailored to the nature of the infection. TLRs are able to distinguish among double-stranded and single-stranded RNA, unmethylated CpG DNA, bacterial lipopolysaccharide (LPS), lipoproteins, flagellin as well as synthetic analogs of various natural products and endogenous ligands such as chromatin-IgG complexes. (see TLR Ligand Table) TLR2 and TLR4 are the best characterized and recognize the microbial motifs PGN (peptidoglycan)/lipoproteins/dectin and LPS, respectively. These PAMPs are expressed within the pathogen cell wall and are accessible for TLR recognition once they come into contact with the cell surface. TLR1 and TLR6 form heterodimers with TLR2 for the discrimination of triacylated lipoproteins from diacylated lipoproteins, respectively. TLR5 is responsible for sensing flagella of motile bacterial species, and TLR11 recognizes pathogenic bacteria commonly associated with urinary tract infections such as uropathogenic *E. coli*, as well as a profilin-like protein from the parasite *T. gondii*. TLRs 3, 7, 8, and 9 recognize intracellular pathogen-derived nucleic acid motifs, dsRNA (double-stranded RNA), ssRNA (single-stranded RNA), or DNA delivered to intracellular compartments after the uptake of viruses and other pathogen or infected cells. TLR9 recognizes non-methylated CpG motifs of bacterial and viral DNA. Binding of ligand to TLR is thought to be unidirectional and irreversible, terminated only by endocytic removal from the cell membrane.

TLR Ligands

TLR	PAMPs	DAMPs
TLR1	Triacylated lipoproteins, GPI-anchored proteins	Unknown
TLR2	Lipoproteins, Peptidoglycan, LPS, Zymosan	Heat shock proteins, Necrotic cells, Oxygen radicals, Urate crystals
TLR3	dsRNA, ssRNA	mRNA
TLR4	LPS, Fusion proteins	β-Defensin 2, Heat shock proteins, HMGB1, Extravascular fibrinogen/fibrin, Lung surfactant protein, Minimally modified LDL, Pancreatic elastase
TLR5	Flagellin	Unknown
TLR6	Diacylated lipoproteins, Zymosan	Unknown
TLR7	ssRNA, Imidazoquinolines	RNA immune complexes
TLR8	ssRNA, Imidazoquinolines, G- and U-rich ssRNA oligonucleotides	Unknown
TLR9	Non-methylated CpG-containing oligonucleotide DNA, viral DNA	CpG chromatin-IgG complexes, DNA immune complexes
TLR10	Unknown	Unknown
TLR11	Uropathogenic bacteria, Profilin-like protein	Unknown
TLR12	Unknown	Unknown
TLR13	Unknown	Unknown

Specificity through Expression, Subcellular Localization, and Signaling

Specificity of TLR signaling comes through dimerization, adaptor combinations, downstream pathway bifurcations and expression within specialized cell types. TLRs are expressed by various cell types including professional immune cells and Tregs (CD4+CD25+ T cells), as well as synovial fibroblast-like cells, epithelial cells and all major glial cell types.[2,3] The TLR family members are either expressed at the cell surface for extracellular ligand (lipid and protein PAMPs) recognition (these include TLRs 1, 2, 4-6, 11-13) or are localized in intracellular compartments such as the endosome, lysosome, or endoplasmic reticulum for detecting bacterial and viral nucleic acid PAMPs (TLRs 3, 7, 8, and 9). TLRs function through dimerization and oligomerization, associating with fellow TLRs or other co-receptors. Most TLRs appear to function as homodimers, though, as noted above, TLR2 forms heterodimers with TLR1 or TLR6, each dimer having different ligand specificity. TLRs may also depend on other co-receptors for full ligand sensitivity. For example, TLR4 recognition of LPS requires MD-2. CD14 and LPS-binding protein (LBP) facilitate the presentation of LPS to MD-2.

TLR signaling involves a sequence of stimulus-induced conformational changes in the receptor. Activation is a sequential process where ligand binding induces conformational change in the C-terminal region of the extracellular domain, which stabilizes TLR-TLR interactions and, in turn, induces conformational changes in the TLR transmembrane domains. When a pathogen is identified by TLR receptor engagement, activated TLR recruits adapter molecules within the cytoplasm of cells in order to propagate a signal. Four adapter molecules are known to be involved in signaling:

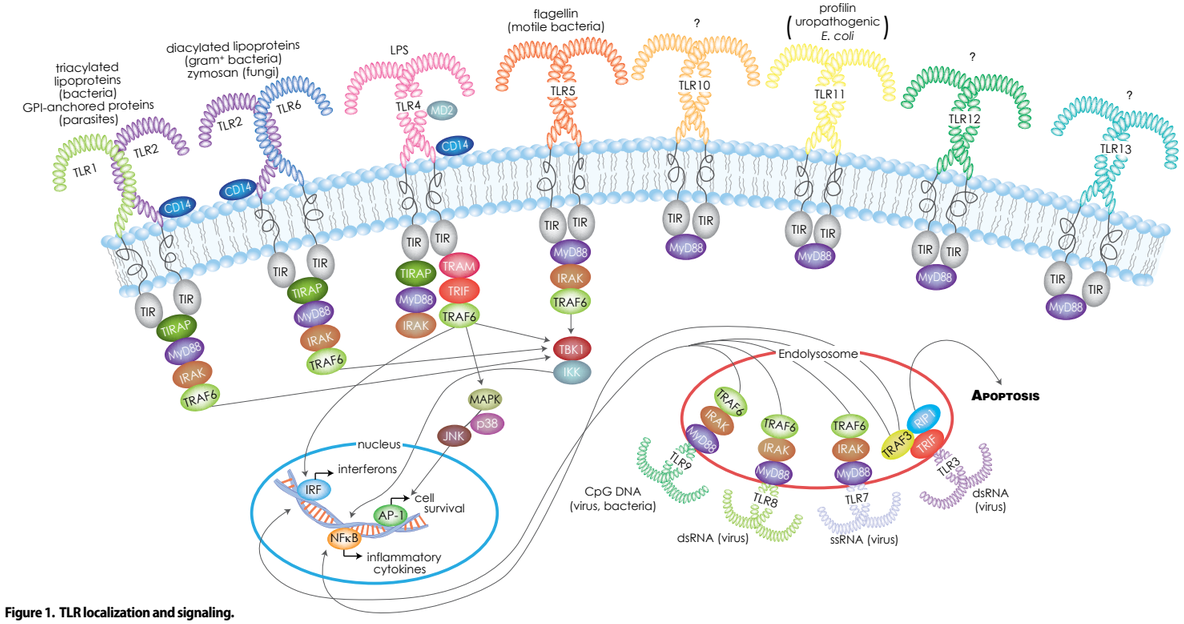


Figure 1. TLR localization and signaling.

MyD88 (myeloid differentiation primary response gene 88), TIRAP (Toll/IL-1 receptor (TIR) domain-containing adaptor protein), TRIF (TIR domain-containing adapter inducing IFN-β), and TRAM (TRIF-related adaptor molecule). These adapters activate certain protein kinases (IRAK (interleukin-1 receptor-associated kinase) 1, IRAK4, TBK1 (TNF-receptor associated factor (TRAF) family member-associated NFκB activator (TANK)-binding kinase), and IKK (IκB kinase)) that amplify the signal, leading to the induction or suppression of multiple genes that coordinate an inflammatory response to eliminate infectious agents.

All TLRs, with the exception of TLR3, recruit MyD88. Additionally, TLRs 1, 2, 4, and 6 recruit the additional adaptors CD14, which is required for LPS binding, and TIRAP, which links the conserved C-terminal intracellular TIR domain with MyD88. In the MyD88-dependent pathway, the MyD88 death domain recruits IRAK, which interacts with the adaptor protein TRAF6 and provides a link to NIK (NFκB-inducing kinase). NIK then phosphorylates IKK, leading to IκB phosphorylation. IκB phosphorylation targets the protein for ubiquitination and proteasome mediated degradation, resulting in the release and nuclear translocation of NF-κB. The MyD88 dependent pathway also facilitates expression of MAPK such as p38 and JNK, and transcription factors, such as interferon regulatory factors (IRFs), influencing the production of a wide array of pro-inflammatory mediators, including reactive oxygen/nitrogen intermediates, cytokines, and chemokines.

TLR3 ligands initiate the TRIF-dependent pathway, whereas TLR4 can signal *via* either MyD88-dependent or TRIF-dependent pathways requiring the additional linker adaptor TRAM in order to associate with TRIF. In the TRIF-dependent pathway, TRIF interacts with TRAF3 to activate IRF3 and IRF7 and initiate IFN-α and IFN-β production, which are hallmarks of the host innate immune response to viral infection. Alternatively, TRIF can also bind to RIP1 (receptor-interacting protein 1) and TRAF6, and activate NF-κB for late-phase induction of inflammatory gene expression or MAPK to increase expression of anti-apoptotic proteins such as AP-1 and Bcl2 family members. TLRs promote both cell death and cell survival signaling pathways. Cell survival pathways might be activated, for example, to prolong the lifespan of usually short-lived polymorphonuclear neutrophils (PMN) to increase their effectiveness against pathogens, whereas cell death activation can be an effective means to kill microbes, preventing their spread throughout the rest of the organism. Because thousands of genes are activated by TLR signaling, the TLRs constitute one of the most pleiotropic yet tightly regulated gateways for gene modulation. Kawai and Akira, 2011 offer a more thorough review of the current understanding of TLR trafficking and signaling.[4]

TLRs in Disease

Prolonged or excessive signaling through TLRs may lead to destructive inflammatory responses that ultimately result in exacerbating infection and undermining the very immune response that was intended to be protective. The presence of DAMPs, like viral ss-RNA, can stimulate TLRs that activate resident immune cells to initiate and propagate inflammation and autoimmunity. Also, TLRs can recognize endogenous self-antigens and generate an aggressive autoimmune response in tissues. A crucial point in the generation of autoimmune disease is represented by defective apoptotic cell clearance that can lead to development of antinuclear antibodies. Inappropriate response of specific TLRs has been implicated in certain autoimmune diseases, immunodeficient diseases, inflammatory disorders, dementia, and cancer. For example, activation of TLR2, 4, 7, and 9 plays a role in experimental allergic encephalomyelitis (EAE), a mouse model of multiple sclerosis (MS), while TLR3 activation protects from this disease.[5] TLR4, 7, and 9 have been connected to both human and mouse models of systemic lupus erythematosus (SLE) and lupus-like syndromes.[6] Furthermore, expression of TLR2, 4, 5, 7, and 9 is also increased in brain tissue of Alzheimer's disease patients and Alzheimer's transgenic mouse models.[7]

Much is still to be determined toward understanding how TLR-mediated responses are tailored to produce either beneficial or detrimental effects, as well as how this signaling pathway can be harnessed for therapeutic benefit.[8,9] Cayman's growing TLR product line contains several helpful research tools, including antibodies that recognize receptors and adaptor proteins. To see all of Cayman's TLR product line please see page 50.

References

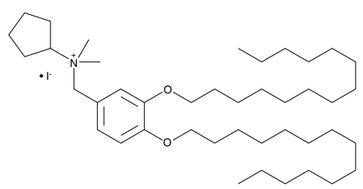
1. Siegmund-Schultze, N. Dtsch Arztebl **104 (16)** A-1072 / B-954 / C-908 (2007).
2. Marques, R. and Boneca, I.G. *Cell Mol. Life Sci.* **68(22)**, 3661-3673 (2011).
3. Abreu, M.T. *Nature Reviews Immunol.* **10,** 131-144 (2010).
4. Kawai T. and Akira S. *Immunity* **34(5)**, 637-650 (2011).
5. Gambuzza M., Licata N., Palella E., *et al. J Neuroimmunol.* **239(1-2)**, 1-12 (2011).
6. Guggino, G. Giardina, A.R., Ciccia, F., *et al. Clinical & Dev. Immunol.* 2012, Article ID 135932 (2012).
7. Hanke, M.L. and Kielian, T. *Clin. Sci.* **121,** 367-387 (2011).
8. Zhu, J. and Mohan, C. *Mediators of Inflammation* 2010, Article ID 781235 (2010).
9. Hedayat M., Netea M.G., and Rezaei N. *Lancet Infect Dis.* **11(9),** 702-712 (2011).

Toll-Like Receptor Signaling

CAY10614 13615

[1202208-36-3]
MF: $C_{42}H_{78}INO_2$ **FW:** 756.0 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An antagonist of lipid A activation of TLR4 (IC_{50} = 1.68 µM), in a cell-based assay; significantly improves survival of mice given intraperitoneal LPS

1 mg
5 mg
10 mg
25 mg



DcR2 Polyclonal Antibody 160755

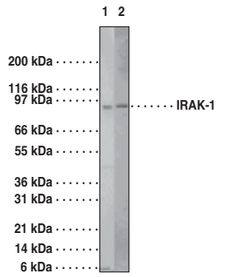
TRAIL-R4, TRUNDD
100 µg affinity-purified IgG in 200 µl PBS containing 0.02% sodium azide
Stability: ≥1 year at 4°C
Summary: Antigen: human DcR2 precursor amino acids 249-263 • Host: rabbit • Cross Reactivity: (+) human DcR2 • Application(s): WB • DcR2 has an extracellular TRAIL-binding domain but lacks an intracellular death domain and does not induce apoptosis. Like DR4 and DR5, DcR2 transcript is widely expressed in normal human tissues. Overexpression of DcR2 attenuates TRAIL-induced apoptosis.

1 ea

IRAK-1 Polyclonal Antibody 13843

Interleukin-1 Receptor-Associated Kinase 1
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 IL-1 response. It mediates a signaling cascade leading to NF-κB activation by members of the IL-1 family including IL-1 and IL-18.

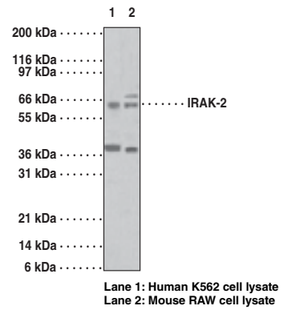
1 ea



IRAK-2 Polyclonal Antibody 13844

Interleukin-1 Receptor-Associated Kinase-Like 2
Protein G-purfied 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 Ser/Thr protein kinase whose primary amino acid sequence shares similarity with that of Pelle, a protein kinase that is essential for the activation of the NF-κB homolog in *Drosophila*. IRAK mediates NF-κB activation by members of the IL-1 family including IL-1 and IL-18.

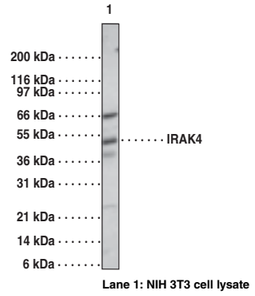
1 ea



IRAK-4 Polyclonal Antibody 13845

Interleukin-1 Receptor-Associated Kinase-Like 4
Protein G-purified IgG **Stability:** ≥6 months at 4°C
Summary: Antigen: synthetic peptide corresponding to a mixture of mouse 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 may act as an upstream activator of IRAK-1 and is important for LPS activation of 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



MyD88 Polyclonal Antibody 13746

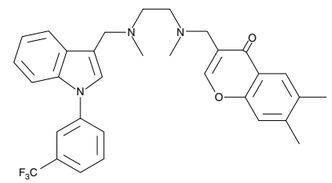
Peptide affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human MyD88 amino acid 233-248 • Host: rabbit • Cross Reactivity: (+) human, mouse, and rat MyD88 • Application(s): WB • MyD88 is a central adapter protein involved in IL-1 and TLR-mediated signaling.

1 ea

SPD-304 10008012

[869998-49-2]
MF: $C_{32}H_{32}F_3N_3O_2$ **FW:** 547.6 **Purity:** ≥98%
A crystalline solid **Stability:** ≥1 year at -20°C
Summary: An inhibitor of TNFα that prevents binding to the TNF Receptor 1 (TNFR1) (IC_{50} = 22 µM)

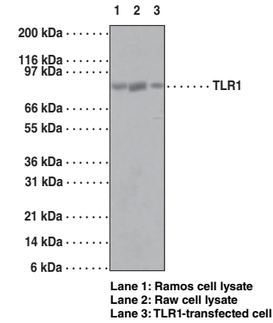
500 µg
1 mg
5 mg
10 mg



Toll-Like Receptor 1 Polyclonal Antibody 13582

Protein G-purified **Stability:** ≥1 year at -20°C
Summary: Antigen: peptide from human TLR1 within the region of amino acids 400-450 • Host: rabbit • Cross Reactivity: (+) human, mouse, and rat TLR1 • Application(s): FC (intracellular and cell surface) and WB • TLR1 interacts with TLR2 and coexpression of TLR1 and TLR2 enhances the NF-κB activation in response to a synthetic lipopeptide. Together, they recognize the lipid configuration of the native mycobacterial lipoprotein as well as several triacylated lipopeptides.

1 ea



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

Protein G-purified **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 interacts with TLR1 and coexpression of TLR1 and TLR2 enhances the NF-κB activation in response to a synthetic lipopeptide. Together, they recognize the lipid configuration of the native mycobacterial lipoprotein as well as several triacylated lipopeptides.

1 ea

Toll-Like Receptor 3 Monoclonal Antibody (Clone 40C1285.6) 13588

Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human TLR3 amino acids 55-70 • Host: mouse, clone 40C1285.6 • Cross Reactivity: (+) human and canine TLR3 • Application(s): FC (intracellular and cell surface), ICC, IHC, IP, and WB • TLR3 has a restricted expression pattern being expressed in dendritic cells. The expression of TLR3 in a single cell type may indicate a specific role for this molecule in a restricted setting.

1 ea

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

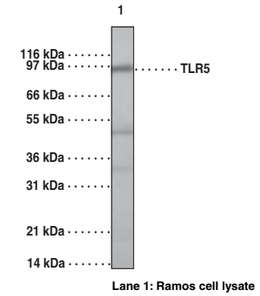
Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: Ba/F3 cell line expressing human TLR4 cell surface antigen • Isotype: IgG_{2aK} • Host: mouse, clone HTA125 • Cross Reactivity: (+) human and canine TLR4 • Application(s): FC (intracellular and cell surface), ICC, IP, and neutralization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

1 ea

Toll-Like Receptor 5 Monoclonal Antibody (Clone 85B152.5) 13595

Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: peptide corresponding to a portion of human TLR5 • Isotype: IgG_{2a} • Host: mouse, clone 85B152.5 • Cross Reactivity: (+) canine, human, and mouse TLR5 • Application(s): FC (intracellular and cell surface) and WB • TLR5 expression is upregulated following exposure to bacteria or to the TLR5 agonist, flagellin. Gram-negative bacteria stimulate monocyte/macrophage cells in a TLR5-specific, CD14-independent manner. TLR5 thus appears to be the principal means by which the innate immune system recognizes flagellated bacterial pathogens.

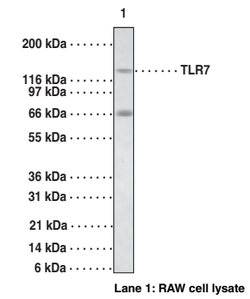
1 ea



Toll-Like Receptor 7 Polyclonal Antibody 13591

Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human TLR7 amino acids 706-728 • Host: rabbit • Cross Reactivity: (+) human, mouse, and rat TLR7 • Application(s): FC (intracellular and cell surface), ICC, IHC (frozen and paraffin), IP, and WB • Stimulation of the NF-κB signaling pathway by TLR7 suggests that it plays a role in immune response.

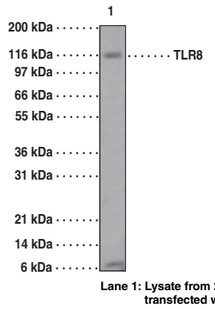
1 ea



Toll-Like Receptor 8 Monoclonal Antibody (Clone 44C143) 13592

Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: peptide from human TLR8 within the region of amino acids 750-850 • Host: mouse, clone 44C143 • Cross Reactivity: (+) human and mouse TLR8 • Application(s): FC (intracellular and cell surface), IHC (paraffin-embedded sections), and WB • TLRs mediate innate immunity that is essential for microbial recognition. The TLR8 gene contains three exons, two of which have coding function.

1 ea

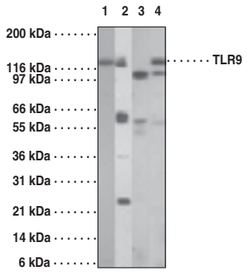


Lane 1: Lysate from 293 cells transfected with human TLR8

Toll-Like Receptor 9 Monoclonal Antibody (Clone 26C593.2) 13593

Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: human TLR9 amino acids 268-284 • Host: mouse, clone 26C593.2 • Cross Reactivity: (+) canine, equine, human, mouse, rat, and Rhesus monkey TLR9 • Application(s): FC (intracellular and cell surface), ICC, IHC (frozen and paraffin), and WB • Gene knockout experiments suggest that TLR9 acts as a receptor for unmethylated CpG dinucleotides in bacterial DNA. TLR9 is highly expressed in spleen.

1 ea



Lane 1: Human PBMCs
Lane 2: Human intestine
Lane 3: Mouse intestine
Lane 4: Rat intestine

Toll-Like Receptor 10 Monoclonal Antibody (Clone 3C10C5) 11111

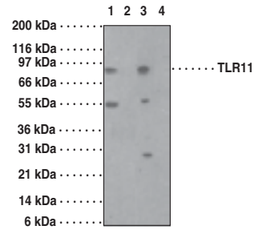
CD290
200 µl of PBS **Stability:** ≥6 months at -20°C
Summary: Antigen: human TLR10 containing amino acids 20-474 • Host: mouse, clone 3C10C5 • Cross Reactivity: (+) human TLR10 • Application(s): FC • TLR10, originally identified from a spleen cDNA library, is on chromosome 4p14 and has been found to be expressed in spleen, thymus, lymph nodes, lung, and in B-lymphocytes.TLR10 is thought to be a potential asthma candidate gene because early life innate immune responses to ubiquitous inhaled allergens and PAMPs may influence asthma susceptibility.

1 ea

Toll-Like Receptor 11 Polyclonal Antibody 13585

Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: mouse TLR11 amino acids 911-926 • Host: rabbit • Cross Reactivity: (+) mouse and rat TLR11 • Application(s): FC (intracellular) and WB • Humans encode a TLR11 gene but it contains several stop codons so that the protein is not expressed. However, mouse and rat TLR11 are functional. TLR11 does not respond to known TLR ligands but instead responds specifically to uropathogenic bacteria. TLR11-deficient mice are highly susceptible to infection of the kidneys by uropathogenic bacteria, indicating that TLR11 may play a protective role in preventing infection of internal organs of the urogenital system.

1 ea



Lane 1: Mouse testis lysate (Absence of immunizing peptide)
Lane 2: Mouse testis lysate (Presence of immunizing peptide)
Lane 3: Rat testis lysate (Absence of immunizing peptide)
Lane 4: Rat testis lysate (Presence of immunizing peptide)

Toll-Like Receptor 12 Polyclonal Antibody 13586

Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: mouse TLR12 amino acids 911-926 • Host: rabbit • Cross Reactivity: (+) mouse and rat TLR12 • Application(s): FC (intracellular) and WB • TLR12 displays a distinct pattern of expression in macrophages, liver, kidney, and bladder epithelial cells. TLR12 does not respond to known TLR ligands.

1 ea

TRAF2 Monoclonal Antibody (Clone 33A1293) 10855

Protein G-purified IgG **Stability:** ≥6 months at -20°C
Summary: Antigen: fusion protein corresponding to amino acids 205-222 of human TRAF2 • Host: mouse • Cross Reactivity: (+) human TRAF2 • Application(s): WB • TRAF2, an adaptor protein that mediates signal transduction from TNF receptors, is involved in cellular resistance to TNF-induced apoptosis. Mutagenic studies suggest that the N-terminal RING finger and two adjacent zinc fingers of TRAF2 are required for NF-κB activation, whereas interaction with TNFR is mediated through the C-terminal domain. Distinct domains in the N- and C-termini are also required for association with TRAF1 and protein kinase receptor interacting protein (RIP).

100 µg

TRAF3 Polyclonal Antibody 10872

Protein G-purified IgG **Stability:** ≥6 months at -20°C
Summary: Antigen: human TRAF3 amino acids 323-340 • Host: rabbit • Cross Reactivity: (+) human and mouse TRAF3 • Application(s): WB • TRAF3, an adaptor protein that mediates signal transduction from TNF receptors, interacts directly with the CD40 cytoplasmic tail through a region of similarity to the TNFα receptor-associated factors. TRAF3 binds only a single site, which contains the sequence PEQET.

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 • TRAF5, an adaptor protein that mediates signal transduction from TNF receptors, is implicated in NF-κB 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. Targeted disruption of TRAF5 gene causes defects in CD40-CD27 mediated lymphocyte activation.

1 ea

TRAF6 Polyclonal Antibody 10874

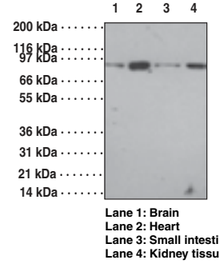
TNF Receptor-Associated Factor 6
Protein G-purified IgG **Stability:** ≥6 months at -20°C
Summary: Antigen: human TRAF6 amino acids 436-449 • Host: rabbit • Cross Reactivity: (+) human and mouse TRAF6 • Application(s): WB • TRANCE/OPGL activates the antiapoptotic Ser/Thr kinase Akt/PKB through a signaling complex involving c-Src and TRAF6, an adaptor protein that mediates signal transduction from TNF receptors. TRAF6 is essential for perinatal and postnatal survival, bone metabolism, and LPS and cytokine signaling.

1 ea

TRAF6BP Polyclonal Antibody 10894

T6BP, TAX1-binding protein, TAX1BP1, TRAF6 Binding Protein
Protein G-purified IgG **Stability:** ≥6 months at -20°C
Summary: Antigen: human TRAF6BP amino acids 718-735 • Host: rabbit • Cross Reactivity: (+) human TRAF6BP • Application(s): WB • A TRAF-interacting protein that associates with TRAF6 in the presence of the IRAK. T6BP shares an overall 50% identity and 59% similarity to chicken protein MDP62, which has been implicated in promoting neurite outgrowth.

1 ea



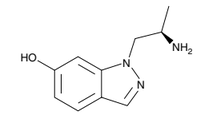
Lane 1: Brain
Lane 2: Heart
Lane 3: Small intestine
Lane 4: Kidney tissue lysate

Synaptic Receptor Signaling

AL 34662 10011546

[210580-75-9] AL 34497
MF: $C_{10}H_{13}N_3O$ **FW:** 191.2 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent 5-HT_2 receptor agonist with ocular hypotensive activity; binds to the human and rat 5-HT_2 receptors in cerebral cortex homogenates with IC_{50} values of 1.5 and 0.77 nM, respectively; lowers IOP 25% at a dose of 100 µg and 33% at 300 µg at six hours post dose

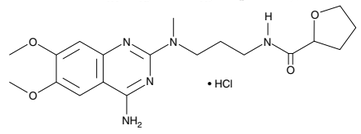
1 mg
5 mg
10 mg
50 mg



Alfuzosin (hydrochloride) 13648

[81403-68-1] SL 77499-10, Uroxatral
MF: $C_{19}H_{27}N_5O_4$ • HCl **FW:** 425.9 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A post-synaptic α_1-adrenergic receptor antagonist commonly used to improve lower urinary tract symptoms associated with benign prostatic hyperplasia; displays high-affinity with non-selectivity for the three known human α_1 adrenoceptors (pK_i = 8.0, 8.0, and 8.5 for α_{1A}, α_{1B}, and α_{1D}, respectively)

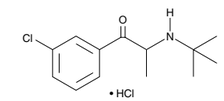
10 mg
50 mg
100 mg
500 mg



Bupropion (hydrochloride) 10488

[31677-93-7] NSC 315851
MF: $C_{13}H_{18}ClNO$ • HCl **FW:** 276.2 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An inhibitor of the reuptake of dopamine and norepinephrine (IC_{50} = 6.5 and 3.4 µM, respectively); also an antagonist of neuronal acetylcholine nicotinic receptors, blocking $\alpha_3\beta_2$ better than $\alpha_4\beta_2$ and α_7 (IC_{50} = 1.3, 8, and 60 µM, respectively)

100 mg
250 mg
500 mg
1 g

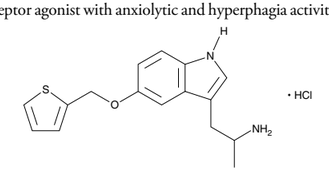


•Also Available: **Bupropion-d_9 (hydrochloride)** (10010679)

BW 723C86 70090

[160521-72-2]
MF: $C_{16}H_{18}N_2OS$ • HCl **FW:** 322.9 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A selective 5-HT_{2B} receptor agonist with anxiolytic and hyperphagia activity

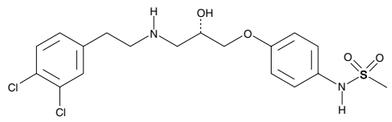
1 mg
5 mg
10 mg
50 mg



CAY10608 13358

[457897-92-6]
MF: $C_{18}H_{22}Cl_2N_2O_4S$ **FW:** 433.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A propanolamine that potently, selectively, and non-competitively antagonizes the NR2B subunit of NMDA receptors (IC_{50} = 50 nM); does not inhibit other NMDA subunits, AMPA receptors, or kainate receptors; has neuroprotective effects *in vitro* and *in vivo*

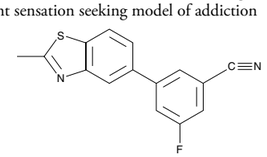
1 mg
5 mg
10 mg
25 mg



CAY10651 10820

MF: $C_{15}H_9FN_2S$ **FW:** 268.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A noncompetitive antagonist of mGlu5 (IC_{50} = 61 nM; K_i = 477 nM); 10 µM results in a near complete blockade of the glutamate response in cortical astrocytes; 30 mg/kg in mice yields potent inhibition in a marble burying model of anxiety and is efficacious in an operant sensation seeking model of addiction

1 mg
5 mg
10 mg
25 mg



DARPP-32 (Phospho-Thr[34]) Polyclonal Antibody 10603

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

1 ea

Dopamine Transporter (C-Term) Polyclonal Antibody 10009372

DAT
Peptide affinity-purified antibody **Stability:** ≥1 year at -20°C
Summary: Antigen: peptide from the C-terminal region of human DAT • Host: rabbit • Cross Reactivity: human, mouse, and Macaque monkey DAT • Application(s): IHC and WB • DAT is responsible for the reaccumulation of dopamine after it has been released. DAT antibodies are widely used as markers for dopaminergic and noradrenergic neurons.

1 ea

$GABA_A$ Receptor δ-subunit (N-Term) Polyclonal Antibody 10600

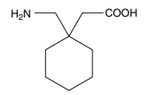
γ-Aminobutyric Acid A Receptor
Affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: fusion protein from the N-terminus of the δ-subunit of rat $GABA_A$ receptor • Host: rabbit • Cross Reactivity: (+) mouse and rat $GABA_A$ Receptor • Application(s): IHC, IP, and WB • $GABA_A$-Rs are important therapeutic targets for a range of sedative, anxiolytic, and hypnotic agents and are implicated in several diseases including epilepsy, anxiety, depression, and substance abuse. It is a multimeric subunit complex with six α's, four β's, and four γ's, plus alternative splicing variants of some of these subunits. Several studies demonstrate that the δ-subunit of the receptor may affect subunit assembly and may also confer differential sensitivity to neurosteroids and to ethanol.

1 ea

Gabapentin 10008346

[60142-96-3] Neurontin®
MF: $C_9H_{17}NO_2$ **FW:** 171.2 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A GABA analogue that acts as an anticonvulsant with proven analgesic effects in various neuropathic pain syndromes

10 mg
25 mg
50 mg
100 mg



GluR1 (Phospho-Ser[831]) Polyclonal Antibody 10602

Glutamate Receptor Subunit 1
Affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: phosphopeptide corresponding to amino acid residues surrounding phospho-Ser^{831} of GluR1 • Host: rabbit • Cross Reactivity: (+) rat GluR1 • Application(s): WB • The AMPAR are comprised of four distinct GluR subunits designated (GluR1-4), which play key roles in virtually all excitatory neurotransmission in the brain. The GluR1 subunit is potentiated by phosphorylation at Ser^{831} which has been shown to be mediated by either PKC or CaM kinase II. Phosphorylation of this site has also been linked to synaptic plasticity as well as learning and memory.

1 ea

GluR1 (Phospho-Ser[845]) Polyclonal Antibody 10601

Glutamate Receptor Subunit 1
Affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: phosphopeptide corresponding to amino acid residues surrounding phospho-Ser^{845} of GluR1 • Host: rabbit • Cross Reactivity: (+) rat GluR1 • Application(s): IHC and WB • The AMPAR are comprised of four distinct GluR subunits designated (GluR1-4), which play key roles in virtually all excitatory neurotransmission in the brain. The GluR1 subunit is potentiated by phosphorylation at Ser^{845} which has been shown to be mediated by either PKC or CaM kinase II. Phosphorylation of this site has also been linked to synaptic plasticity as well as learning and memory.

1 ea

Glycine Receptor Polyclonal Antibody 10009399

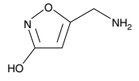
Peptide affinity-purified antibody **Stability:** ≥1 year at -20°C
Summary: Antigen: peptide from N-terminal region of the α_1-subunit of the rat glycine receptor • Host: rabbit • Cross Reactivity: (+) human, mouse, and rat glycine receptor • Application(s): IHC (frozen sections) and WB • Glycine is an important inhibitory neurotransmitter whose binding to its receptor produces a large increase in chloride conductance, which causes membrane hyperpolarization. Glycine receptors are anchored at inhibitory chemical synapses. They have been used to great advantage in the identification of the binding sites for alcohol and have also been extremely useful in studies of synaptic clustering of receptors.

1 ea

Muscimol 13667

[2763-96-4] Agarin, Pantherine
MF: $C_4H_6N_2O_2$ **FW:** 114.1 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A full $GABA_A$ agonist and partial $GABA_C$ agonist; binds $GABA_A$ on both high- and low-affinity sites (K_d = 10 and 270 nM, respectively), stimulating chloride efflux with an EC_{50} vaule of 200 nM; activates $GABA_C$ receptors with an EC_{50} value of 1.3 µM; impairs memory formation and retrieval; attenuates airway constriction

5 mg
10 mg
25 mg



NMDA Receptor NR1 Subunit Monoclonal Antibody 10607

Affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: fusion protein containing amino acids 1-564 of the NR1 subunit of rat NMDA receptor • Host: mouse • Cross Reactivity: (+) rat and mouse NMDA receptor • Application(s): IP and WB • The NMDAR plays an essential role in memory, neuronal development and it has also been implicated in several disorders of the central nervous system including Alzheimer's, epilepsy and ischemic neuronal cell death. The NR1 protein can form NMDA activated channels when expressed in *Xenopus oocytes* but the currents in such channels are much smaller than those seen *in situ*.

1 ea

NMDA Receptor NR2A Subunit Polyclonal Antibody 10608

Affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: fusion protein from the C-terminus of the NR2A subunit of rat NMDA receptor • Host: rabbit • Cross Reactivity: (+) human, rat, and mouse NMDA receptor • Application(s): IHC, IP, and WB • The NMDAR plays an essential role in memory, neuronal development and it has also been implicated in several disorders of the central nervous system including Alzheimer's, epilepsy and ischemic neuronal cell death. Channels with physiological activity are produced when the NR1 subunit is combined with one or more of the NMDAR2 (NR2 A-D) subunits.

1 ea

NMDA Receptor NR2B Subunit Polyclonal Antibody 10609

N-methyl-D-aspartate Receptor
Affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: fusion protein from the C-terminus of the NR2B subunit of rat NMDA receptor • Host: rabbit • Cross Reactivity: (+) human, rat, and mouse NMDA receptor • Application(s): IHC, IP, and WB • Overexpression of the NR2B-subunit of the NMDA receptor has been associated with increases in learning and memory while aged, memory impaired animals have deficiencies in NR2B expression.

1 ea

NMDA Receptor NR2B Subunit (Phospho-Tyr[1252]) Polyclonal Antibody 10009759

Peptide-affinity purified **Stability:** ≥1 year at -20°C
Summary: Antigen: phosphopeptide corresponding to amino acid residues surrounding phospho-Tyr^{1252} of the human NMDA Receptor NR2B Subunit • Host: rabbit • Cross Reactivity: (+) human and rat NMDA receptor; expected to react with bovine, canine, chicken, mouse, non-human primates, and zebrafish NMDA receptor • Application(s): WB • Phosphorylation of Tyr^{1252} in NR2B is thought to potentiate NMDA receptor-dependent influx of calcium.

1 ea

NMDA Receptor NR2B Subunit (Phospho-Tyr[1336]) Polyclonal Antibody 10009760

Peptide-affinity purified **Stability:** ≥1 year at -20°C
Summary: Antigen: phosphopeptide corresponding to amino acid residues surrounding phospho-Tyr^{1336} of the human NMDA Receptor NR2B Subunit • Host: rabbit • Cross Reactivity: (+) human and rat NMDA receptor; expected to react with bovine, canine, chicken, mouse, non-human primates, and zebrafish NMDA receptor • Application(s): WB • Phosphorylation of Tyr^{1336} in NR2B is thought to potentiate NMDA receptor-dependent influx of calcium. Ischemia may also increase the phosphorylation of this site.

1 ea

NMDA Receptor NR2B Subunit (Phospho-Tyr[1472]) Polyclonal Antibody 10009761

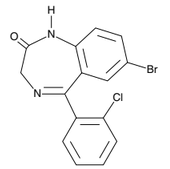
Peptide-affinity purified **Stability:** ≥1 year at -20°C
Summary: Antigen: phosphopeptide corresponding to amino acid residues surrounding phospho-Tyr^{1472} of NMDA Receptor NR2B Subunit • Host: rabbit • Cross Reactivity: (+) human and rat NMDA receptor; expected to react with bovine, canine, chicken, mouse, non-human primates, and zebrafish NMDA receptor • Application(s): WB • Phosphorylation of Tyr^{1472} on NR2B may regulate the functional expression of the receptor in LTP and other forms of plasticity.

1 ea

Phenazepam 9000849

[51753-57-2] BD 98, Fenazepam
MF: $C_{15}H_{10}BrClN_2O$ **FW:** 349.6 **Purity:** ≥98%
A crystalline solid **Stability:** ≥1 year at -20°C
Summary: A benzodiazepine agonist of the $GABA_A$-benzodiazepine receptor chloride channel complex; has been shown to exhibit strong anxiolytic, sedative, anticonvulsive, and hypnotic properties; has been shown to act as an anxioselective tranquilizer at very low doses (10-5 to 10-10 mg/kg)

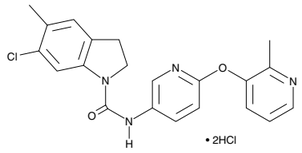
5 mg
10 mg
25 mg
100 mg



SB 242084 (hydrochloride) 10096

[1049747-87-6]
MF: $C_{21}H_{19}ClN_4O_2$ • 2HCl **FW:** 467.8 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An antagonist of the 5-HT_{2C} receptor (pK_i = 9.0), with at least 100-fold more selectivity over other 5-HT, dopamine, or adrenergic receptors; brain penetrant with significant anxiolytic activity; used extensively in animal research

1 mg
5 mg
10 mg
25 mg



Ion Channel Signaling

A-803467 10012588

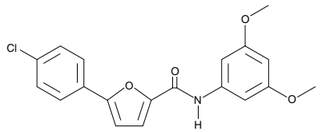
[944261-79-4]

MF: $C_{19}H_{16}ClNO_4$ **FW:** 357.8 **Purity:** ≥98%

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

Summary: A sodium channel blocker with high-affinity and selectivity for inhibiting human $Na_v1.8$ sodium channels (IC_{50} = 8 nM when stimulated at half-maximal inactivation and IC_{50} = 79 nM at a resting state); dose dependently reduces behavioral responses in a variety of neuropathic and inflammatory pain models

5 mg
10 mg
50 mg
100 mg



Capsaicin 92350

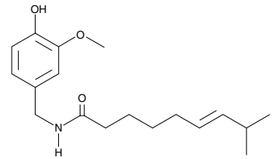
[404-86-6]

MF: $C_{18}H_{27}NO_3$ **FW:** 305.4 **Purity:** ≥95%

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

Summary: Primary active component of the heat and pain-eliciting lipid-soluble fraction of the capsicum pepper

50 mg
100 mg
250 mg
1 g



•Also Available: **Capsaicin (technical grade)** (10010743)

Capsazepine 10007518

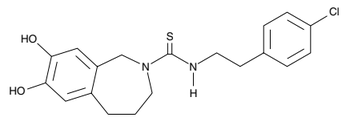
[138977-28-3]

MF: $C_{19}H_{21}ClN_2O_2S$ **FW:** 376.9 **Purity:** ≥98%

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

Summary: A competitive TRPV1 antagonist which blocks capsaicin-induced uptake of Ca^{2+} in neonatal rat dorsal root ganglia (IC_{50} = 0.42 µM) and CHO cells (IC_{50} = 17 nM)

1 mg
5 mg
10 mg
50 mg



$Ca_v1.2$ Calcium Channel Monoclonal Antibody (Clone S57-46) 13702

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

Summary: Antigen: fusion protein amino acids 1,507-1,733 • Isotype: IgG_{2b} • Host: mouse, clone S57-46 • Cross Reactivity: (+) human, mouse, and rat $Ca_v1.2$ • Application(s): ICC, IF, IHC, and WB • $Ca_v1.2$ is a cardiac L-type calcium channel important for excitation and contraction of the heart.

100 µg

$Ca_v1.3$ Calcium Channel Monoclonal Antibody (Clone S38-8) 13703

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

Summary: Antigen: fusion protein amino acids 2,025-2,161 (C-terminal) of rat $Ca_v1.3$ • Isotype: IgG_1 • Host: mouse, clone S38-8 • Cross Reactivity: (+) human, mouse, and rat $Ca_v1.3$ • Application(s): ICC, IF, IHC, and WB • $Ca_v1.3$ subunits are primarily expressed in neurons and neuroendocrine cells and potentially in heart atria and may figure prominently in atrial arrhythmias. $Ca_v1.3$ also carries the primary sensory receptors of the mammalian cochlea and also expressed in the electromotile outer hair cells.

100 µg

$Ca_v1.3$ Calcium Channel Monoclonal Antibody (Clone S48A-9) 13706

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

Summary: Antigen: fusion protein amino acids 859-875 (N-terminal) of human $Ca_v1.3$ • Isotype: IgG_{2a} • Host: mouse, clone S48A-9 • Cross Reactivity: (+) human, mouse, and rat $Ca_v1.3$ • Application(s): ICC, IHC, and WB • $Ca_v1.3$ subunits are primarily expressed in neurons and neuroendocrine cells and potentially in heart atria and may figure prominently in atrial arrhythmias. $Ca_v1.3$ also carries the primary sensory receptors of the mammalian cochlea and also expressed in the electromotile outer hair cells.

100 µg

$Ca_v3.2$ Calcium Ion Channel Monoclonal Antibody (Clone S55-10) 13704

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

Summary: Antigen: fusion protein amino acids 1,019-1,293 (II-III loop) human $Ca_v3.2$ • Isotype: IgG_1 • Host: mouse, clone S55-10 • Cross Reactivity: (+) human, mouse, and rat $Ca_v3.2$ • Application(s): ICC, IHC, and WB • $Ca_v3.2$ is a protein encoded by the CACNA1H gene, which is associated with childhood absence epilepsy. Studies suggest that the up-regulations of $Ca_v3.2$ may participate in the progession of prostate cancer toward an androgen-independent stage.

100 µg

$Ca_v\beta1$ Calcium Channel Monoclonal Antibody (Clone S7-18) 13700

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

Summary: Antigen: rat $Ca_v\beta1$ amino acids 19-34 • Isotype: IgG_{2a} • Host: mouse, clone S7-18 • Cross Reactivity: (+) human, mouse, and rat $Ca_v\beta1$ • Application(s): ICC, IHC, and WB • $Ca_v\beta1$ plays an important role in the calcium channel by modulating G protein inhibition, increasing peak calcium current, controlling the α1 subunit membrane targeting and shifting the voltage dependence of activation and inactivation.

100 µg

$Ca_v\beta4$ Calcium Channel Monoclonal Antibody (Clone S10-7) 13701

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

Summary: Antigen: rat $Ca_v\beta4$ amino acids 458-474 • Isotype: IgG_1 • Host: mouse, clone S10-7 • Cross Reactivity: (+) human, mouse, and rat $Ca_v\beta4$ • Application(s): ICC, IF, IHC, and WB • $Ca_v\beta4$ plays an important role in calcium channel function by modulating G protein inhibition, increasing peak calcium current, controlling the α1 subunit membrane targeting and shifting the voltage dependence of activation and inactivation.

100 µg

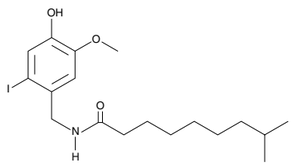
CAY10448 10005633

MF: $C_{18}H_{28}INO_3$ **FW:** 433.3 **Purity:** ≥98%

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

Summary: A potent VR_1 antagonist (IC_{50} ~ 10 nM)

1 mg
5 mg
10 mg
50 mg



Dihydrocapsaicin 92355

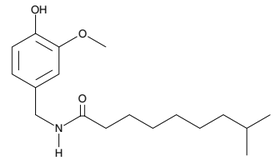
[19408-84-5]

MF: $C_{18}H_{29}NO_3$ **FW:** 307.4 **Purity:** ≥98%

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

Summary: Represents about 10% of the compound present in commercial preparations purporting to be pure capsaicin; potency at VR_1 appears equivalent to capsaicin

5 mg
10 mg
50 mg
100 mg



HCN1 Cyclic Nucleotide-gated Channel Monoclonal Antibody (Clone S70-28) 13705

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

Summary: Antigen: fusion protein amino acids 778-910 (cytoplasmic C-terminus) of rat HCN1 • Host: mouse, clone S70-28 • Isotype: IgG_1 • Cross Reactivity: (+) human, mouse, and rat HCN1 • Application(s): ICC, IHC, IP, and WB • Hyperpolarization-activated cation channels of the HCN gene family, such as HCN1, play a crucial role in the regulation of cell excitability. Importantly, they contribute to spontaneous rhythmic activity in both the heart and brain.

100 µg

HCN2 Cyclic Nucleotide-gated Channel Monoclonal Antibody (Clone S71-37) 13707

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

Summary: Antigen: fusion protein amino acids 761-863 (cytoplasmic C-terminus) of rat HCN2 • Host: mouse, clone S71-37 • Isotype: IgG_1 • Cross Reactivity: (+) human and rat HCN2 • Application(s): ICC, IHC, IP, and WB • Hyperpolarization-activated cation channels of the HCN gene family contribute to spontaneous rhythmic activity in both the heart and the brain.

100 µg

HCN3 Cyclic Nucleotide-gated Channel Monoclonal Antibody (Clone S141-28) 13708

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

Summary: Antigen: fusion protein amino acids 660-779 (cytoplasmic C-terminus) of mouse HCN3 • Host: mouse, clone S141-28 • Isotype: IgG_1 • Cross Reactivity: (+) mouse and rat HCN3 • Application(s): ICC, IHC, and WB • Hyperpolarization-activated cation channels of the HCN gene family contribute to spontaneous rhythmic activity in both the heart and the brain.

100 µg

HCN4 Cyclic Nucleotide-gated Channel Monoclonal Antibody (Clone S114-10) 13709

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

Summary: Antigen: fusion protein amino acids 1,019-1,108 (cytoplasmic C-terminus) of rat HCN4 • Host: mouse, clone S114-10 • Isotype: IgG_1 • Cross Reactivity: (+) human, mouse, and rat HCN4 • Application(s): ICC, IHC, and WB • Hyperpolarization-activated cation channels of the HCN gene family contribute to spontaneous rhythmic activity in both the heart and the brain.

100 µg

Icilin 10137

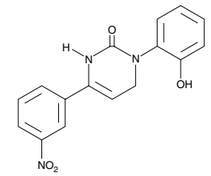
[36945-98-9] AG 3-5

MF: $C_{16}H_{13}N_3O_4$ **FW:** 311.3 **Purity:** ≥98%

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

Summary: A synthetic CMR1/TRPM8 super agonist that is 2.5-fold more efficacious and nearly 200-fold more potent than the reference cold thermosensory agonist, l-menthol

1 mg
5 mg
10 mg
50 mg



Ionomycin 10004974

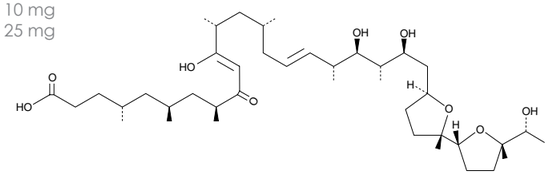
[56092-81-0]

MF: $C_{41}H_{72}O_9$ **FW:** 709.0 **Purity:** ≥98%

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

Summary: A selective calcium ionophore that mobilizes intracellular calcium stores. It is used as a research tool to raise the intracellular level of calcium, to study calcium transport across biological membranes, and to stimulate the intracellular production of cytokines

1 mg
5 mg
10 mg
25 mg



KCNQ1 Potassium Channel Monoclonal Antibody (Clone S37A-10) 13711

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

Summary: Antigen: fusion protein amino acids 2-101 of human KCNQ1 • Host: mouse, clone S37A-10 • Isotype: IgG_1 • Cross Reactivity: (+) human, mouse, and rat KCNQ1 • Application(s): ICC, IHC, IP, and WB • $K_v7.1$ (K_vLQT1) is a potassium channel protein coded by the gene KCNQ1. $K_v7.1$ is present in the cell membranes of cardiac muscle tissue and in inner ear neurons among other tissues. In the cardiac cells, $K_v7.1$ mediates the IKs (or slow delayed rectifying potassium) current that contributes to the repolarization of the cell, terminating the cardiac action potential and thereby the heart's contraction.

100 µg

KCNQ2 Potassium Channel Monoclonal Antibody (Clone S26A-23) 13712

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

Summary: Antigen: fusion protein amino acids 1-59 of human KCNQ2 • Host: mouse, clone S26A-23 • Isotype: IgG_1 • Cross Reactivity: (+) human, mouse, and rat KCNQ2 • Application(s): ICC, IHC, IP, and WB • $K_v7.1$ (K_vLQT1) is a potassium channel protein coded by the gene KCNQ1. It is associated with benign familial neonatal convulsions.

100 µg

KCNQ4 Potassium Channel Monoclonal Antibody (Clone S43-6) 13713

Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: fusion protein amino acids 2-77 of human KCNQ4 • Host: mouse, clone S43-6 • Isotype: IgG_1 • Cross Reactivity: (+) human, mouse, and rat KCNQ4 • Application(s): ICC, IP, and WB • The protein encoded by this gene forms a potassium channel that is thought to play a critical role in the regulation of neuronal excitability, particularly in sensory cells of the cochlea. The current generated by this channel is inhibited by M_1 muscarinic acetylcholine receptors and is activated by retigabine, a novel anti-convulsant drug.

100 µg

$K_{ir}2.1$ Potassium Channel Monoclonal Antibody (Clone S21-32) 13714

Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: fusion protein amino acids 41-64 and 189-428 of mouse $K_{ir}2.1$ • Host: mouse, clone S21-32 • Isotype: IgG_1 • Cross Reactivity: (+) human, mouse, and rat $K_{ir}2.1$ • Application(s): IHC and WB • The $K_{ir}2.1$ inward-rectifier potassium ion channel is encoded by the KCNJ2 gene. A defect in this gene is associated with Andersen-Tawil syndrome.

100 µg

$K_{ir}2.2$ Potassium Channel Monoclonal Antibody (Clone S24-1) 13715

Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: fusion protein amino acids 362-427 of mouse $K_{ir}2.2$ • Host: mouse, clone S24-1 • Isotype: IgG_1 • Cross Reactivity: (+) human, mouse, and rat $K_{ir}2.2$ • Application(s): IHC and WB • $K_{ir}2.2$ participates in establishing action potential waveform and excitability of neuronal and muscle tissues. This gene encodes an inwardly rectifying potassium ion channel which may be blocked by divalent cations. This protein is thought to be one of multiple inwardly rectifying channels which contribute to the cardiac inward rectifier current (IK1).

100 µg

$K_{ir}2.3$ Potassium Channel Monoclonal Antibody (Clone S25-35) 13716

Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: fusion protein amino acids 390-445 of human $K_{ir}2.3$ • Host: mouse, clone S25-35 • Isotype: IgG_1 • Cross Reactivity: (+) human, mouse, and rat $K_{ir}2.3$ • Application(s): IHC and WB • $K_{ir}2.3$ is an integral membrane protein and member of the inward rectifier potassium channel family. The encoded protein has a small unitary conductance compared to other members of this protein family.

100 µg

$K_v3.1b$ Potassium Channel Monoclonal Antibody (Clone S16B-8) 13717

Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: fusion protein amino acids 437-585 of rat $K_v3.1b$ • Host: mouse, clone S16B-8 • Isotype: IgG_1 • Cross Reactivity: (+) human, mouse, and rat $K_v3.1b$ • Application(s): IHC and WB • $K_v3.1b$ has been extensively tested in the auditory regions of mammals, and the decline of $K_v3.1b$ expression appears to correlate with the functional decline in the medial olivocochlear efferent system. Other research shows potential for $K_v3.1b$ channels to be oxygen sensors.

100 µg

$Na_v1.7$ Sodium Channel Monoclonal Antibody (Clone S68-6) 13718

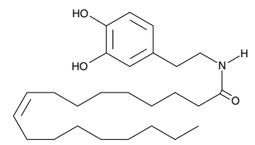
Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: fusion protein amino acids 1,751-1,946 of rat $Na_v1.7$ • Isotype: IgG_1 • Host: mouse, clone S68-6 • Cross Reactivity: (+) human, mouse, and rat $Na_v1.7$ • Application(s): ICC, IP, and WB • $N_{av}1.7$ is a voltage-gated sodium channel that plays a critical role in the generation and conduction of action potentials and is thus important for electrical signaling by most excitable cells.

100 µg

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)

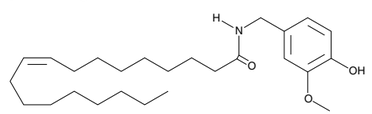
5 mg
10 mg
50 mg
100 mg



Olvanil 90262

[58493-49-5] NE 19550, N-Vanillyloleamide
MF: $C_{26}H_{43}NO_3$ **FW:** 417.6 **Purity:** ≥98%
A solution in ethanol **Stability:** ≥2 years at -20°C
Summary: A structural analog of capsaicin and an VR_1 agonist that induces desensitization analgesia in rat and mouse models of pain; potentiates the agonist activity of endogenous CBs by inhibiting the reuptake of AEA

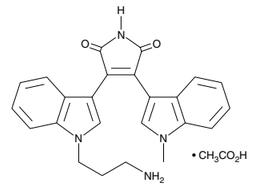
5 mg
10 mg
25 mg
50 mg



Ro 31-7549 (acetate) 13333

[138516-31-1] Bisindolylmaleimide VIII
MF: $C_{24}H_{22}N_4O_2 \bullet C_2H_4O_2$ **FW:** 458.5 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A selective PKC inhibitor (IC_{50} = 158 nM for rat brain PKC) that acts at the ATP binding site of PKC; exhibits PKC isozyme specificity with preference for PKCα over PKCβI, PKCβII, PKCγ, or PKCε (IC_{50}s = 53, 195, 163, 213, and 175 nM, respectively)

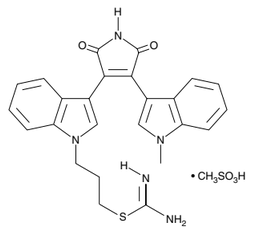
1 mg
5 mg
10 mg
25 mg



Ro 31-8220 (mesylate) 13334

[138489-18-6] Bisindolylmaleimide IX
MF: $C_{25}H_{23}N_5O_2S \bullet CH_4O_3S$ **FW:** 553.7 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent, cell-permeable inhibitor of PKC isoforms (IC_{50} = 5, 24, 14, 27, and 24 nM for PKC-α, PKC-βI, PKC-βII, PKC-γ, and PKC-ε, respectively)

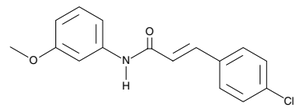
1 mg
5 mg
10 mg
50 mg



SB 366791 11019

[472981-92-3]
MF: $C_{16}H_{14}NO_2$ **FW:** 287.7 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A selective TRPV1 antagonist widely used in pain research; inhibits capsaicin-evoked Ca^{2+} influx with an IC_{50} value of 0.7 µM in cultured trigeminal ganglion neurons; reduces capsaisin-induced nociceptive responses in a model of pain and suppresses tolerance to the analgesic effects of chronic morphine administration in rats

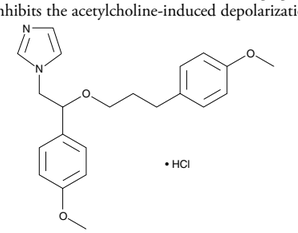
5 mg
10 mg
25 mg
50 mg



SKF-96365 (hydrochloride) 10009312

[130495-35-1]
MF: $C_{22}H_{26}N_2O_3 \bullet HCl$ **FW:** 402.9 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An inhibitor of receptor-mediated influx of calcium *via* voltage-gated calcium channels (IC_{50} ~ 10 µM); inhibits the acetylcholine-induced depolarization of circular smooth muscle

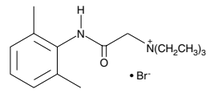
1 mg
5 mg
10 mg
50 mg



QX-314 (bromide) 10011032

[24003-58-5]
MF: $C_{16}H_{27}N_2O \bullet Br$ **FW:** 343.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A membrane-impermeant lidocaine derivative that when combined with capsaicin selectively blocks sodium channels on nociceptive neurons *via* the TRPV1 channel; decreases the pain response without imparting numbness or paralysis associated with other local anesthetics

1 mg
5 mg
10 mg
25 mg



TRPC4 Calcium Channel Monoclonal Antibody (Clone S77-15) 13719

Transient Receptor Potential Cation Channel
Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: rat TRPC4 amino acids 930-947 • Isotype: IgG_{2b} • Host: mouse, clone S77-15 • Cross Reactivity: (+) human, mouse, and rat TRPC4 • Application(s): ICC, IP, and WB • TRPC4 is expressed in smooth muscle and endothelial cells where it regulates membrane potential and calcium influx. TRPC4 is activated by G_q/phospholipase C-coupled receptors.

100 µg

TRPM7 Ion Channel Ser/Thr Kinase Monoclonal Antibody (Clone S74-25) 13720

Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: fusion protein amino acids 1,817-1,863 of mouse TRPM7 • Isotype: IgG_1 • Host: mouse, clone S74-25 • Cross Reactivity: (+) human, mouse, and rat TRPM7 • Application(s): ICC, IP, and WB • TTRP-PLIK is a protein that is both an ion channel and a kinase. As a channel, it conducts calcium and monovalent calcium. As a kinase, it is capable of phosphorylating itself and other substrates. The kinase activity is necessary for channel function.

100 µg

TRPV3 Channel Monoclonal Antibody (Clone S15-4) 13721

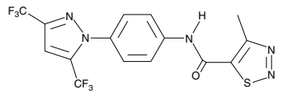
Protein G-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: amino acids 458-474 of rat TRPV3 • Isotype: IgG_{2a} • Host: mouse, clone S15-4 • Cross Reactivity: (+) human, mouse, and rat TRPV3 • Application(s): ICC, IP, and WB • TRPV3 plays a role in temperature sensation and vasoregulation. It is expressed in a subset of sensory neurons that terminate in the skin and is activated at temperatures between 22 and 40°C. The gene lies in close proximity to the TRPV1 gene on chromosome 17, and the two encoded proteins are thought to associate with each other to form heteromeric channels.

100 µg

YM-58483 13246

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

1 mg
5 mg
10 mg
25 mg

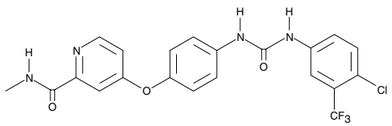


Downstream Kinase Signaling

BAY-43-9006 10009644

[284461-73-0] Nexovar®, Sorafenib
MF: $C_{21}H_{16}ClF_3N_4O_3$ **FW:** 464.8 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: An inhibitor of Raf-1 and B-Raf (IC_{50} = 6 and 22 nM, respectively), as well as several receptor tyrosine kinases, including VEGFR- 2 and -3, PDGFR-β, Flt-3, and c-KIT (IC_{50} = 90, 15, 20, 57, and 58 nM); inhibits tumor angiogenesis and induces tumor cell apoptosis, particularly in renal cell carcinoma and hepatocellular carcinoma

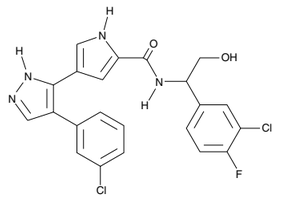
1 mg
5 mg
10 mg
50 mg



CAY10561 10010043

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

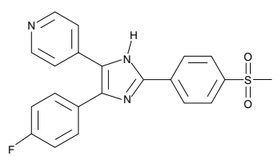
500 µg
1 mg
5 mg
10 mg



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 Ser/Thr kinase homologous to p38, inhibiting its kinase activity (IC_{50} = 0.03 µM)

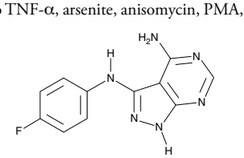
5 mg
10 mg
25 mg
100 mg



CGP 57380 13322

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

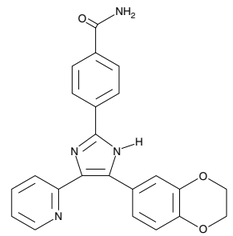
1 mg
5 mg
10 mg
25 mg



D 4476 13305

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

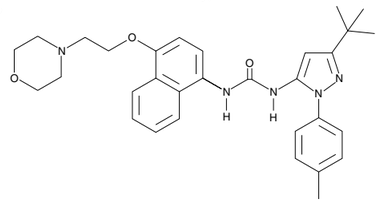
1 mg
5 mg
10 mg
50 mg



Doramapimod 10460

[285983-48-4] BIRB-796
MF: $C_{31}H_{37}N_5O_3$ **FW:** 527.7 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A highly potent inhibitor of p38 MAPK (K_d = 0.1 µM) that blocks TNFα release in LPS-stimulated THP.1 cells with an IC_{50} value of 18 nM; at 10 µM, inhibits JNK2α2 *in vitro*

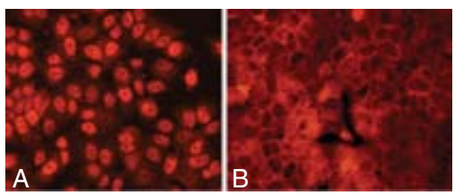
1 mg
5 mg
10 mg
25 mg



ERK/MAPK (Phospho-Thr^{202}/Tyr^{204}) Cell-Based Phosphorylation/Translocation Assay Kit 10010549

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

1ea



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

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

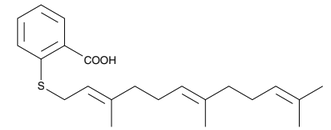
Affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: phosphopeptide corresponding to amino acid residues surrounding the phospho-Thr^{202} and phospho-Tyr^{204} of rat ERK/MAPK • Host: rabbit • Cross Reactivity: (+) human and rat ERK/MAPK • Application(s): WB • ERK/MAPK is an integral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

1 ea

Farnesyl Thiosalicylic Acid 10010501

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

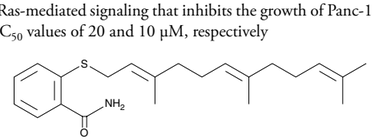
1 mg
5 mg
10 mg
25 mg



Farnesyl Thiosalicylic Acid Amide 13175

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

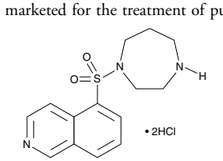
1 mg
5 mg
10 mg
50 mg



HA-1077 (hydrochloride) 10010559

[203911-27-7] AT-877, Eril, Fasudil
MF: $C_{14}H_{17}N_3O_2S$ • 2HCl **FW:** 364.3 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A potent inhibitor of ROCK-II, PRK-2, MSK1, and MAPKAP-K1b with IC_{50} values of 1.9, 4, 5, and 15 µM, respectively; reduces blood vessel constriction, decreases pulmonary arterial pressure, inhibits tumor angiogenesis, and improves insulin signaling in a diabetic rat model; marketed for the treatment of pulmonary arterial hypertension and stable angina

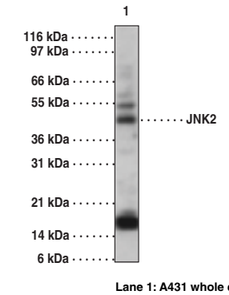
5 mg
50 mg
100 mg



JNK2 Polyclonal Antibody 11511

c-Jun Amino Terminal Kinase 2, MAPK9 antibody, p54a, SAPK1a
Peptide affinity-purified **Stability:** ≥6 months at -20°C
Summary: Antigen: human JNK2 amino acids 373-389 • Host: rabbit • Cross Reactivity: (+) human JNK2 • Application(s): WB • JNK2, along with JNK1 and JNK3, are MAP kinase family members thought to play an important role in nuclear signal transduction through environmental stress activation and subsequent phosphorylation of the nuclear transcription factor p53. IMG-586 recognizes JNK2.

1 ea



Lane 1: A431 whole cell lysate (20 µg)

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

MAP Kinase Kinase 1, MAPK1
Affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: phosphopeptide corresponding to amino acid residues surrounding Phospho-Thr^{292} of human MEK1 • Host: rabbit • Cross Reactivity: (+) human and rat MEK1; expected to react with bovine, canine, chicken, mouse, non-human primates, and *Xenopus* MEK1 • Application(s): WB • MEK1 is an integral component of the MAPK cascade that regulates cell growth and differentiation. MEK1 is phosphorylated by MAPK on Thr^{292} and Thr^{386}.

1 ea

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

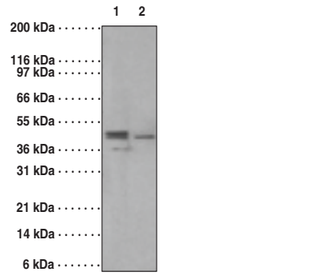
MAP Kinase Kinase 1, MAPK1
Affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: phosphopeptide corresponding to amino acid residues surrounding Phospho-Thr^{386} of human MEK1 • Host: rabbit MEK1 • Cross Reactivity: (+) rat MEK1 • Application(s): WB • MEK1 is an integral component of the MAPK cascade that regulates cell growth and differentiation. MEK1 is phosphorylated by MAPK on Thr^{292} and Thr^{386}.

1 ea

MEK1/2 Polyclonal Antibody 13846

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

1 ea



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

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

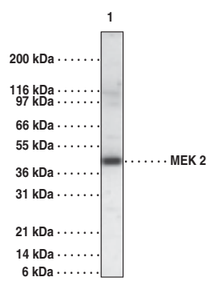
MAP Kinase Kinase 1/2, MAPKK1/2
Affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: phosphopeptide corresponding to amino acid residues surrounding phospho-$Ser^{218,222}$ of human MEK1/2 • Host: rabbit • Cross Reactivity: (+) NIH 3T3 cells • Application(s): WB • MEK1 is an integral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

1 ea

MEK2 Polyclonal Antibody 13847

Dual Specificity MAP Kinase Kinase 2, MAP Kinase/ERK Kinase 2, MAP Kinase Kinase 2, MAPKK2
Affinity-purified IgG **Stability:** ≥6 months at -20°C
Summary: Antigen: peptide from human MEK2 • Host: rabbit • Cross Reactivity: (+) human MEK2 • Application(s): WB • Human MEK2 is activated through phosphorylation of its serine residues at positions 222 and 226 by a variety of cytokines and growth factors. It is responsible for the phosphorylation/activation of MAP kinases and ERKs, and is an essential component in the transduction of mitogenic signals.

1 ea

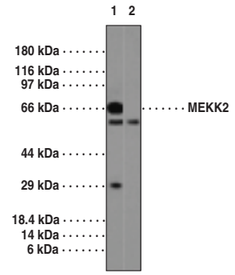


Lane 1: 293 cell lysate

MEKK2 Polyclonal Antibody 13848

Dual Specificity MAP Kinase Kinase Kinase 2, MAP3K2, MAP Kinase/ERK Kinase Kinase 2, MAP Kinase Kinase Kinase 2, MAPKKK2
Protein G-purified IgG **Stability:** ≥6 months at -20°C
Summary: Antigen: peptide within the region of human MEKK2 amino acids 1-50 • Host: rabbit • Cross Reactivity: (+) human MEKK2 • Application(s): IHC (paraffin embedded-sections) and WB • MEKK2 directly phosphorylates and activates IκB kinases. It regulates T-cell function, controls cytokine gene expression in mast cells, mediates EFGR and fibroblast growth factor-2 receptor signals, and plays a role in rheumatoid arthritis.

1 ea

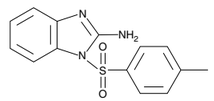


Lane 1: Human liver cell lysate (absence of immunizing peptide)
Lane 2: Human liver cell lysate (presence of immunizing peptide)

Nodinitib-1 11040

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

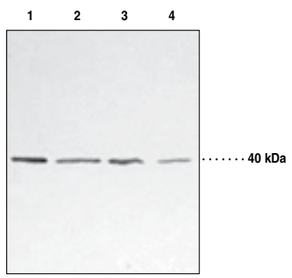
5 mg
10 mg
25 mg
50 mg



p38 MAPK Monoclonal Antibody (Clone 9F12) 10011301

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

1 ea

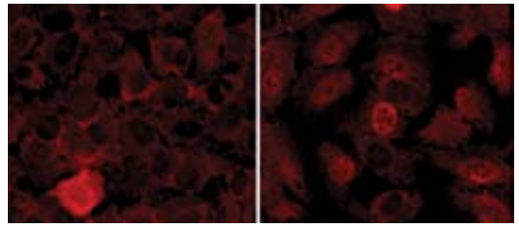


Lane 1: Human platelet lysate (25 µg)
Lane 2: Jurkat cell lysate (25 µg)
Lane 3: RAW 264.7 cell lysate (50 µg)
Lane 4: Rat heart supernatant (25 µg)

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

Stability: ≥1 year at -20°C
Summary: p38 MAPK is activated by phosphorylation at Thr^{180} and Tyr^{182} in response to both inflammatory cytokines and stress. The subcellular location of p38 following stimulation is not well understood. Cayman's p38 Cell-Based Phosphorylation/Translocation Assay provides a highly specific phospho-p38 MAPK (phospho-Thr^{180} and Tyr^{182}) primary antibody together with a Dylight™ (product of Thermo Scientific) conjugated secondary antibody in a ready-to-use format. Thrombin, for treatment of cells, is included as a positive control.

1ea


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

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

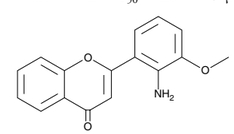
Anti-Phospho-Thr^{180}/Tyr^{182} p38 MAPK
Affinity-purified IgG **Stability:** ≥1 year at -20°C
Summary: Antigen: phosphopeptide corresponding to amino acid residues surrounding phospho-Thr^{180} and phospho-Tyr^{182} of rat p38 MAPK • Host: rabbit • Cross Reactivity: (+) human p38 MAPK • Application(s):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

500 µl

PD 98059 10006726

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

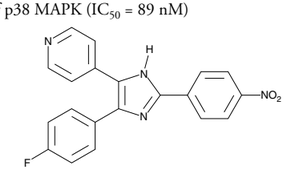
1 mg
5 mg
10 mg
50 mg



PD 169316 10006727

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

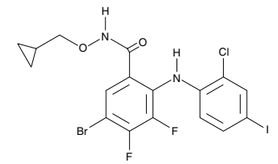
1 mg
5 mg
10 mg
25 mg



PD 184161 10012431

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

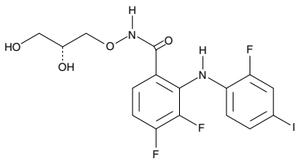
1 mg
5 mg
10 mg
25 mg



PD 0325901 13034

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

1 mg
5 mg
10 mg
25 mg



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

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

1 ea

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

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

1 ea

Ribosomal S6 Kinase 2 Polyclonal Antibody 10009411

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

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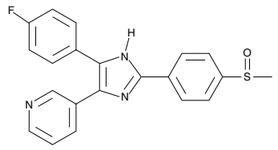
SB 203580 — 13067

[152121-47-6] PB 203580, RWJ 64809
MF: $C_{21}H_{16}FN_3OS$ **FW:** 377.4 **Purity:** ≥98%
A crystalline solid **Stability:** ≥2 years at -20°C
Summary: A specific, pyridinyl imidazole inhibitor of p38 MAPK that inhibits p38 MAPK activity (IC_{50} = 0.6 µM)

5 mg
10 mg
50 mg
100 mg

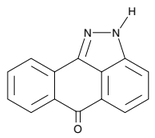


•Also Available: **SB 203580 (hydrochloride)** (13344)

SP 600125 — 10010466

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

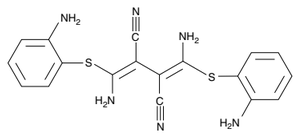
5 mg
10 mg
25 mg
50 mg



U-0126 — 70970

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

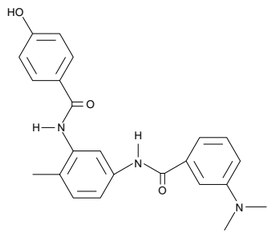
1 mg
5 mg
10 mg
50 mg



ZM 336372 — 10010367

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

1 mg
5 mg
10 mg
25 mg



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