Pain Research

The development of novel pain therapeutics relies on understanding the highly complex nociceptive signaling pathways. Cayman offers a select group of tools to study TRP ion channels, purinergic receptors, voltage-gated ion channels, and various G protein-coupled receptors (GPCRs) that are known to be expressed by nociceptive primary afferent nerves. Modulators of glutamate, GABA, and nicotinic acetylcholine receptors are also available.

Pain Transmission

Primary nociceptor afferents release neurotransmitters such as glutamate and prostaglandins, which bind to specific receptors on the postsynaptic membrane to transmit a pain signal.

The antinociceptive response includes inhibitory interneurons, signaling *via* GABA receptors, that activate μ-opioid receptors, among others.

Inhibitory pathways descending from the brainstem release neurotransmitters such as serotonin (5-HT) or activate small opioid-containing interneurons in the spinal dorsal horn to release opioid peptides.

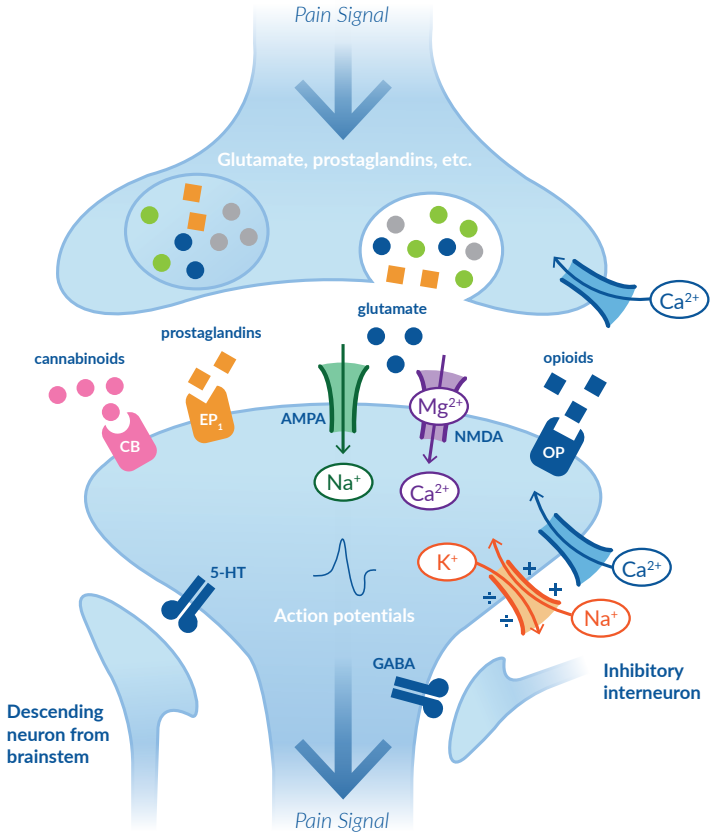


Image adapted from: Olesen, A.E., Andresen, T., Staahl, C., *et al. Pharmacol. Rev.* **64(3)**, 722-779 (2012).

Ligand-Gated Ion Channels

TRP Ion Channel Agonists and Antagonists

Item No.	Product Name	Summary
26191	AMG 517	A TRPV1 antagonist (IC_{50} = 0.9 nM)
14715	AMG 9810	A competitive antagonist of capsaicin activation of TRPV1 (IC_{50}s = 24.5 and 85.6 nM for human and rat, respectively)
92350	Capsaicin	The primary heat and pain-eliciting compound of the *Capsicum* pepper
10007518	Capsazepine	A competitive TRPV1 antagonist that blocks the capsaicin-induced uptake of Ca^{2+} (IC_{50} = 0.42 μM in neonatal rat dorsal root ganglia and IC_{50} = 17 nM in Chinese hamster ovary cells)
11923	HC-030031	A selective TRPA1 channel blocker that antagonizes TRPA1-mediated calcium influx induced by AITC and formalin (IC_{50}s = 6.2 and 5.3 μM, respectively)
10137	Icilin	A CMR1/TRPM8 super agonist that serves as the reference cold nociceptive agonist for TRP-type ion channels
20458	JYL1421	A TRPV1 receptor antagonist
21019	Supercinnamaldehyde	A TRPA1 activator (EC_{50} = 0.8 μM)

Glutamate/GABA Receptor Agonists and Antagonists

Item No.	Product Name	Summary
18600	(±)-Baclofen	A selective agonist of $GABA_B$ (IC_{50} = 180 nM)
16355	Gaboxadol (hydrochloride)	A $GABA_A$ receptor agonist whose potency varies depending on the receptor subunit composition
20919	Ganaxolone	A positive modulator of $GABA_A$ receptors containing α_1, α_2, α_3, β_2, and γ_{2L} subunits
15351	LY379268	A brain permeable, selective agonist of mGluR2 and mGluR3
10009019	(+)-MK-801 (hydrogen maleate)	A selective, non-competitive NMDA receptor antagonist (K_i = 30.5 nM)

P2X Receptor Antagonists

Item No.	Product Name	Summary
14580	A-438079 (hydrochloride)	A competitive antagonist of the $P2X_7$ receptor (pIC_{50} = 6.9)
21256	A-740003	A competitive antagonist of the $P2X_7$ receptor (IC_{50}s = 40 and 18 nM for human and rat receptors, respectively)
21895	JNJ-47965567	A selective $P2X_7$ antagonist

Nicotinic Acetylcholine Receptor Modulators

Item No.	Product Name	Summary
21018	NS 1738	A positive allosteric modulator of α7-containing nAChRs
14304	PNU-120596	A positive allosteric modulator of the α7 nAChR, increasing agonist-evoked calcium flux (EC_{50} = 216 nM)
15030	Varenicline (tartrate)	A partial agonist of the α4β2 neuronal nAChR (EC_{50} = 2.3 µM)

Additional modulators of ligand-gated ion channels available at www.caymanchem.com

Voltage-Gated Ion Channels

Sodium Channel Blockers

Item No.	Product Name	Summary
10012588	A-803467	A $Na_v1.8$ sodium channel blocker (IC_{50} = 8 nM when stimulated at half-maximal inactivation and IC_{50} = 79 nM at a resting state)
10011032	QX-314 (bromide)	A selective blocker of sodium channels on nociceptive neurons
21422	(–)-Ropivacaine (hydrochloride hydrate)	A reversible blocker of sodium channels in nerve fibers
14964	Tetrodotoxin (citrate)	A neurotoxic blocker of Na_v channels

Calcium Channels

Item No.	Product Name	Summary
10008346	Gabapentin	Penetrates the central nervous system and blocks the $\alpha_2\delta$-type voltage-gated calcium channels
22475	Mirogabalin	Blocks $\alpha_2\delta$-1 and $\alpha_2\delta$-2 subunits of voltage-dependent calcium channels
9002652	Phenibut (hydrochloride)	Blocks $\alpha_2\delta$ subunit-containing voltage-gated calcium channels

Potassium Blockers

Item No.	Product Name	Summary
15185	ML-213	A selective activator of KCNQ2 and KCNQ4 channels
15191	ML-252 (hydrochloride)	A selective inhibitor of the voltage-gated potassium channel subtype $K_v7.2$ (IC_{50} = 69 nM in a patch clamp assay)
15193	ML-277	An activator of KCNQ1 channels (EC_{50} = 260 nM)
21449	Retigabine	An activator of KCNQ2/3, KCNQ3/5, KCNQ2, KCNQ3, KCNQ4, and KCNQ5 channels (EC_{50}s = 1.6, 1.4, 2.5, 0.6, 5.2, and 6.4 µM, respectively)

Additional modulators of voltage-gated ion channels available at www.caymanchem.com

GPCR Receptors

Prostanoid Signaling

Cayman is the gold standard for manufacturing compounds that target the inflammatory mediators of the arachidonic acid cascade. This includes selective cyclooxygenase (COX) inhibitors, NSAIDs, blockers of microsomal prostaglandin E synthase-1 (mPGES-1), and antagonists of prostaglandin receptors.

COX Inhibitors

Item No.	Product Name	Summary
70260	Aspirin	A non-selective, irreversible COX inhibitor
10008672	Celecoxib	A selective COX-2 inhibitor (IC_{50} = 50 nM)
70280	(±)-Ibuprofen	A non-selective, reversible COX-1 and COX-2 inhibitor (IC_{50}s = 2.6 and 1.53 µM, respectively)
70290	(+)-Naproxen	A non-selective COX inhibitor
20304	Tenoxicam	A COX-2 inhibitor (IC_{50}s = 20 and 322 nM for COX-1 and COX-2, respectively)

A wide range of selective and non-selective COX-1 and -2 inhibitors available at www.caymanchem.com

mPGES-1 Inhibitors

Item No.	Product Name	Summary
13164	CAY10589	A dual mPGES-1 and 5-lipoxygenase inhibitor
13217	MF63	A selective, orally active inhibitor of human mPGES-1 (IC_{50} = 1.3 nM)
18904	PF-9184	An inhibitor of mPGES-1 (IC_{50} = 16.5 nM for recombinant human enzyme)

Additional selective and non-selective mPGES-1 inhibitors as well as dual mPGES-1/lipoxygenase inhibitors available at www.caymanchem.com

Prostaglandin EP_1 Receptor Antagonists

Item No.	Product Name	Summary
14070	ONO-8711	A selective EP_1 receptor antagonist (K_is = 0.6 and 1.7 nM for human and mouse EP_1, respectively)
14060	SC-19220	A selective EP_1 antagonist (IC_{50} = 6.7 µM for displacing radiolabeled PGE_2 from hEP_1)
10010744	SC-51322	A selective EP_1 antagonist with analgesic activity in mouse pain models (ED_{50} = 0.9 mg/kg)

Additional EP_1 selective antagonists available at www.caymanchem.com

Cannabinoid Receptors

The cannabinoid receptors CB_1 and CB_2 can be activated by endogenous cannabinoids, plant cannabinoids, and synthetic cannabinoids to modulate pain perception. Cayman offers a collection of incredibly potent cannabinoid receptor ligands, many of which are highly selective for either the central or peripheral receptor, as well as inhibitors of endocannabinoid transport and enzyme degradation.

Item No.	Product Name	Summary
71670	AM251	A CB_1 receptor antagonist (K_i = 7.5 nM) and GPR55 agonist (EC_{50} = 39 nM)
90060	AM404	A blocker of AEA reuptake with an IC_{50} of 1 µM in rat neurons and 5 µM in rat astrocytes
91054	Arachidonoyl 2'-Chloroethylamide	A stable, selective CB_1 receptor agonist (K_i = 1.4 nM)
90050	Arachidonoyl Ethanolamide	An endogenous cannabinoid (K_is = 61 and 1,940 nM for CB_1 and CB_2, respectively)
14497	JNJ-1661010	A selective FAAH inhibitor (IC_{50}s = 34 and 33 nM in rat and human, respectively)
10005428	JWH 133	A selective CB_2 receptor agonist (K_i = 3.4 and 677 nM for CB_2 and CB_1, respectively)
13158	JZL 184	A selective MAGL inhibitor (IC_{50}s = 8 nM and 4 µM for MAGL and FAAH in mouse brain membranes, respectively)
26791	LY2828360	A selective CB_2 receptor agonist

A complete list of cannabinoid receptor ligands and inhibitors of endocannabinoid reuptake and degradation is available at www.caymanchem.com

Opioid Signaling

Cayman offers specific opioid receptor agonists as well as related analgesics to study pain relief by modulating the signaling of various receptors involved in nociception.

Opioid Receptor Ligands

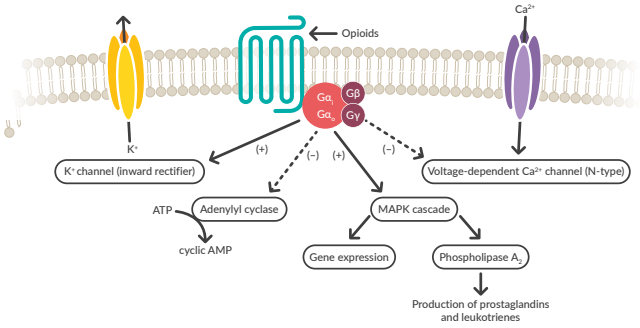
Item No.	Product Name	Summary
26150	AT-121	A dual, partial agonist at μ- and nociceptin-opioid receptors
14025	Buprenorphine (hydrochloride)	A partial agonist at μ- and κ-opioid receptors and an antagonist at δ-opioid receptors
21553	DAMGO	A selective peptide agonist of the μ-opioid receptor (K_i = 1.18 nM for human μ-opioid receptors)
23184	DPDPE (trifluoroacetate salt)	A synthetic peptide δ-opioid receptor agonist (K_i = 2.7 nM)
18169	Dynorphin A	A κ-, μ-, and δ- opioid receptor agonist (K_is = 0.5-1 nM); activates human nociceptin receptor (K_i = 386 nM)
18178	Dynorphin B	A κ_{1b}-opioid receptor agonist (K_i = 1.1 nM)
21254	JTC 801	An antagonist of the nociceptin receptor (K_i = 44.5 nM; IC_{50} = 94 nM)
12037	MCOPPB (hydrochloride)	An agonist for the nociceptin receptor (pK_i = 10.1, EC_{50} = 0.39 nM)
15196	ML-335	An agonist of μ-opioid and δ-opioid receptor heterodimerization (EC_{50} = 403 nM); may alleviate the unwanted effects associated with prolonged opiate use
23186	Nalfurafine	A κ-opioid receptor agonist (EC_{50} = 0.05 nM for human receptors expressed in CHO cell membranes)
15070	Nociceptin	A nociceptin receptor ligand (K_i = 88 μM in CHO cells)
22244	Salvinorin B Mesylate	A selective κ-opioid receptor agonist (EC_{50} = 30 nM)
15599	SNC 80	A nonpeptide δ-opioid receptor agonist (K_i = 0.18 nM; IC_{50} = 2.73 nM)

Additional opioid receptor agonists available at www.caymanchem.com

Non-Opioid Analgesics

Item No.	Product Name	Summary
22928	BD 1047 (hydrobromide)	A selective σ_1 receptor antagonist (K_i = 0.9 nM in a radioligand binding assay)
18933	KT109	A selective DAGLβ inhibitor (IC_{50} = 42 nM)
25682	(R)-KT109	A DAGLβ inhibitor (IC_{50} = 0.79 nM) that is the more potent enantiomer compared to (S)-KT109 (Item No. 25683)
20390	Racecadotril	An enkephalinase inhibitor that prevents the degradation of endogenous opioids
16279	S1RA	A selective σ_1 receptor antagonist (K_i = 17 nM); enhances peripheral μ-opioid analgesia without affecting opioid-induced constipation
21777	ST034307	An adenylyl cyclase 1 inhibitor that reduces hypersensitivity to touch in mouse hind paw (ED_{50} = 0.28 μg)
15600	Thiorphan	A potent inhibitor of neprilysin produced *in vivo via* the metabolism of racecadotril

Additional non-opioid analgesics available at www.caymanchem.com



Read the Article:

Non-Addictive Pain Relief: Promising Strategies for Solving the Opioid Crisis

at www.caymanchem.com/painkillers