The Vanilloid Receptor TRPV1 & Other TRP Channels

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Transient Receptor Potential (TRP) channels constitute a family of cation-permeable channels with members across the phylogenetic tree, from yeast to humans. Most of the proteins in this family display a putative topology of six transmembrane domains with a pore forming loop between the fifth and sixth segment. Based on amino acid sequence homology, the mammalian members of the TRP family have been classified into six subfamilies; TRPC (canonical), TRPV (vanilloid), TRPM (melastatin), TRPML (mucolipin), TRPP (polycystin), and TRPA (ankyrin) [1-3]. TRP channels gate in response to a myriad of stimuli such as mechanical stimuli, natural compounds, temperature, or changes in the lipid bilayer. They are crucially involved in physiological processes such as pain perception, photo-reception, thermal and mechanical nociception, perception of pungent compounds, osmosensation, smooth muscle tone and blood pressure regulation [4-6].

TRPV1
Six vanilloid receptors have been characterized so far (see Table 1). They are all sensory transducers, highly conservative in their transmembrane regions, but heterogenous in their N-terminal amino acid sequences and widely different in their gating mechanism and regulation. The archetypal vanilloid receptor is the transient receptor potential cation channel subfamily V member 1 (TRPV1)-sensitizing stimuli. The red arrows indicate negative regulation by phosphatidylinositol 4,5-bisphosphate (PIP₂), calcium and calmodulin. Receptors and cognate ligands known to mediate the sensitization of TRPV1 are shown on the left. These largely sensitize TRPV1 through protein kinase activation, although increased arachidonic acid metabolite production and PIP₂ hydrolysis are also important. Coloured circles represent amino acid residues that have been identified to be important in particular functions: green: vanilloid binding (Y511, S512, L547, T550); blue: protein kinase phosphorylation sites (S116, T370, S502, T704, S800); grey: low-pH activation (E600, E646). The red line indicates the carboxy-terminal domain of TRPV1, which has been shown to interact with both PIP₂ and calmodulin. Adapted from: The vanilloid receptor TRPV1: 10 years from channel cloning to antagonist proof-of-concept: A. Szallasi, et al.; Nat. Rev. Drug. Discov. 6, 357 (2007)

CONTINUED ON PAGE 2
Introduction

suggested to mediate both thermal and chemical pain. Since then, TRPV1 has been reported to be activated by multiple stimuli such as allicin [10, 11], camphor [12], nitric oxide [13], and venoms from jellyfish and spider [14, 15]. As a transducer for thermal, chemical and mechanical stimuli TRPV1 is expressed in primary afferent nociceptors but can also be found in higher brain centers, as well as various non-neuronal tissues [8, 16]. TRPV1 knock-out animals exhibit normal responses to noxious mechanical stimuli but exhibit a lack of behavioural responses to capsaicin and diminished responses to acute thermal stimuli [17, 18]. In addition, they show reduced thermal hypersensitivity in inflammatory pain models with no significant reduction in the thermal hyperalgesia induced by nerve injury models. These findings present TRPV1 as a polymodal receptor responding predominantly under inflammatory conditions and thus diseased.

Sensitization and Modulation

Recently, different inflammatory mediators such as bradykinin [19], prostaglandins [20], signaling pathways leading to the phosphatidylinositol 3-kinase (PI3K) pathway by which TRPV1 sensitization is modulated has been shown to indirectly sensitize TRPV1. The mechanism by which TRPV1 sensitization is modulated is not yet fully understood. TRPV1 is under the inhibitory control of phosphatidylinositol biphosphate (PIP2) and can be cleaved by phospholipase C (PLC), which is coupled to important pain receptors such as bradykinin B2 receptor [19]. Other mechanisms involve different signalling pathways leading to the phosphorylation of TRPV1 by kinases such as protein kinase A (PKA) [26] and C (PKC) [27, 28]. Dephosphorylation by protein phosphatases such as calcineurin are thought to promote desensitization [29, 30].

Endovanilloids (TRPV1 Agonists)

Endovanilloids are defined as endogenous ligands and activators of TRPV1. The search for such ligands has led to candidate molecular classes including endocannabinoids, N-arachidonoyldopamine, lipoxigenase metabolites of arachidonic acid, and polynamines. Anandamide (AEA), a known agonist of cannabinoid receptors, has been also identified as the first endogenous ligand of TRPV1 [31, 32]. Later, N-arachidonoyldopamine (NADA) was found to activate TRPV1 in the hippocampus [33, N-oleyl-dopamine (OLDA) has been shown to induced hyperalgesic effects [34], and several products of lipoxigenases such as 12(S)-hydroperoxyeicosatetraenoic acid (12(S)-HPETE), 15(S)-hydroperoxyeicosatetraenoic acid (15(S)-HPETE), and leukotriene B4 (LTB4) were found to activate the capsaicin-activated channel in isolated membrane patches of sensory neurons [35].

TRPV1 Antagonists

The area of vanilloid antagonism has been the most active area in medicinal chemistry of vanilloids carried out in industry. The first generation TRPV1 antagonist capsazepine, a weak and only moderately selective agent [36], has long been the only vanilloid antagonist available, whereas the dye ruthenium red is a relatively powerful convulsant whereas the dye ruthenium red is a relatively powerful convulsant whereas the dye ruthenium red is a relatively powerful convulsant where the dye ruthenium red is a relatively powerful convulsant where the dye ruthenium red is a relatively powerful convulsant where the dye ruthenium red is a relatively powerful convulsant where the dye ruthenium red is a relatively powerful convulsant where the dye ruthenium red is a relatively powerful convulsant where the dye ruthenium red is a relatively powerful convulsant where the dye ruthenium red is a relatively powerful convulsant where the dye ruthenium red is a relatively powerful convulsant where the dye ruthenium red is a relatively powerful convulsant where the dye ruthenium red is a relatively powerful convulsant where the dye ruthenium red is a relatively powerful convulsant where the dye ruthenium red is a relatively powerful convulsant where the dye ruthenium red is a relatively powerful convulsant where the dye ruthenium red is a relatively powerful convulsant where the dye ruthenium red is a relatively powerful convulsant where the dye ruthenium red is a relatively powerful.convulsant. Since then, TRPV1 has been reported as a potential target for pain relief.

TABLE 1: TRPV1 nomenclature, synonyms of the vanilloid receptors and their mode of action.

<table>
<thead>
<tr>
<th>New Name</th>
<th>Old Name(s)</th>
<th>Activation</th>
</tr>
</thead>
<tbody>
<tr>
<td>TRPV1</td>
<td>Vanilloid Receptor 1 (VR1)</td>
<td>GOM-likerm Transient Receptor Potential Channel 1 (OTRPRC1)</td>
</tr>
<tr>
<td>TRPV2</td>
<td>Vanilloid Receptor Like 1 (VRL-1)</td>
<td>Growth Factor-regulated Channel (GRC)</td>
</tr>
<tr>
<td>TRPV3</td>
<td>Vanilloid Receptor Like 3 (VRL-3)</td>
<td>T&gt;31°C</td>
</tr>
<tr>
<td>TRPV4</td>
<td>Vanilloid Receptor Like 2 (VRL-2)</td>
<td>GOM-likerm Transient Receptor Potential Channel 4 (OTRPRC4)</td>
</tr>
<tr>
<td>TRPV5</td>
<td>Epithelial Calcium Channel (ECAC)</td>
<td>Calcium Channel 1 (ECAC1)</td>
</tr>
<tr>
<td>TRPV6</td>
<td>Epithelial Calcium Channel (ECAC)</td>
<td>Calcium Transporter (Cat)</td>
</tr>
</tbody>
</table>

Selected Review Articles

The paper lists a variety of review articles and reports on the vanilloid receptor TRPV1.

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Anandamide – Crosstalk between TRPV1 and Cannabinoid Receptors

In 1999, it was reported that anandamide activates TRPV1 receptors on sensory arteries as well as both rat and human TRPV1 in heterologous expression systems. This made this compound the first endogenous ligand for TRPV1 [1,2]. It is widely recognized that anandamide is not stored in vesicles like other mediators but is analogous to other eicosanoids, produced on demand in a Ca^2+ dependent manner [3]. This is the result of a biosynthetic mechanism relying on the existence of a phospholipid precursor for anandamide, and of a Ca^2+-sensitive phosphodiesterase for the conversion of this precursor into anandamide.

Although the biosynthetic route underlying the formation of anandamide has been extensively studied, the phospholipase D (PLD) responsible for release of anandamide from its precursor N-arachidonoylphosphatidylethanolamine has only been purified recently, cloned and characterized [4]. The discovery of crosstalk between TRPV1 ligands and cannabinoids has added a further layer of complexity to the field of cannabinoids and vanillins [5]. The endocannabinoid anandamide shows affinity for the cannabinoid receptor (CB1) and TRPV1. The two receptors are co-expressed in dorsal root ganglia and several areas of the CNS. Furthermore, there is also a partial overlapping between the ligand recognition properties of TRPV1 and the anandamide transporter. Clearly, the endocannabinoid and the vanillins systems are closely related and these discoveries have sparked a heated debate regarding the physiological relevance of this relationship. Although anandamide can activate TRPV1, there are still doubts about whether this compound should be considered a true endovanillinn, since the concentrations required for TRPV1 activation are higher than those needed for CB1 activation. On the other hand, the activity of anandamide is increased in vivo by the phosphorylation of TRPV1 by PKA and further potentiated by the entourage effect of various inactive ethanolamides.

These results synthesized on demand along with anandamide and inhibit its metabolic degradation by the enzyme fatty acid hydrolase (FAAH).

The cannabino-vanillin crosstalk can provide new opportunities for clinical exploitation, since cannabinoid-vanillins could overcome some of the drawbacks of the systemic administration of compounds with pure vanillino activity. Recently, first such cannabinoid-vanillino hybrids have been synthesized [6].

Endovanilloids, TRPV1 Agonists & Related Products

**Oleoylethanolamide**

- **Endocannabinoid. Also inhibits adenylate cyclase (IC50=117nM).** Does also bind to TRPV1 (Kd=5.63µM).

**Eugenol (high purity)**

- **[3-Methoxy-4- (2-pyrogallol)phenyl]**
- **ALX-350-123-G001**
  - 1 g
  - Isolated from clove oil, nutmeg, cinnamon and bay leaf. TRPV1 agonist. Analgesic.

**Evodiamine**

- **ALX-350-330-M10**
  - 10 mg
- **ALX-350-330-M50**
  - 50 mg
- A non-pungent vanilloid receptor agonist isolated from *Evodoa rutaecarpa.*

**R-1 Methanandamide**

- **[(R)-1-(4-Arachidonyl)-1-hydroxy-2-propylamide]**
  - **ALX-340-030-M005**
  - 25 µg
  - *Amidine resistant cannabinoid receptor (CB) agonist (Kd=20nM; CB1; Kd=815nM). The most potent of the series of 4-folding highly binding affinity for cannabinoid receptor CB1 than anandamide (Prod. No. ALX-340-029) in the presence of PMSC. Does also bind to TRPV1 (Kd=4.67µM).

**Leukotriene B4**

- **[17β]-**
- **ALX-340-038-C025**
  - 25 µg

**Linoylethanolamide**

- **[(9Z,12Z)-Hydroperoxy-5Z,8Z,11Z-13E-eicosatetraenoic acid]**
  - **ALX-340-044-M005**
  - 5 mg
  - *Ligand of TRPV1 with low affinity to CB2 receptor (Kd=3.4µM). Also inhibits anandamide uptake (IC50=8.0µM).*

**Linvadin**

- **ALX-340-044-M005**
  - 5 mg

**N-Oleoyldopamine**

- **[OLDA; N-(2-(3,4-Dihydroxyphenyl)ethyl)-9Z-octadecenoic acid]**
- **ALX-350-330-M10**
  - 10 mg
- **ALX-350-330-M50**
  - 50 mg
  - *Endogenous TRPV1 agonist (Kd=36nM, EC50=36nM) with weak affinity for rat CB1, receptor (Kd=1.6µM). Potent inhibitor of S-lepoxigenase (IC50=7.5nM) and of early and late events in TCR mediated T cell activation.*

**Oleylethanolamide**

- **[(9Z)-Hydroperoxy-5Z,8Z,11Z-13E-eicosatetraenoic acid]**
- **ALX-340-045-C025**
  - 25 µg
  - *Amidine resistant cannabinoid receptor (CB) agonist (CB1; Kd=20µM; CB2; Kd=815nM). The most potent of the series of 4-folding high binding affinity for cannabinoid receptor CB1, than anandamide (Prod. No. ALX-340-029) in the presence of PMSC. Does also bind to TRPV1 (Kd=4.67µM).*

**CONTINUED ON PAGE 5**
Endovanilloids, TRPV1 Agonists & Related Products cont.

Ovanil
[NE-19550, N-Vanillylployravamide]

ALX-340-041-M005 5 mg
ALX-340-041-M010 10 mg

Hybrid activator of CB1 receptor (IC50: Kd=1.6µM; CB2-Kd=15µM) and TRPV1 (IC50=0.4µM; EC50=33nM (human); EC50=6.71nM (rat)). Also inhibits anandamide uptake (IC50=2µM; Kd=14.1µM) and fatty acid amide hydrolase (FAAH) (IC50=20µM).


Resiniferatoxintype Phorboid Vanilloids

PDDHV
[Phorbol 12,13-dodecanate 20-homovanillate]

ALX-550-371-M001 1 mg
ALX-550-371-M005 5 mg

Resiniferatoxin-type phorboid vanilloid with capsai- cin-like selectivity for TRPV1 (Kd=60nM).


PDDHV
[Phorbol 12,13-dimcanoate 20-homovanillate]

ALX-550-372-M001 1 mg
ALX-550-372-M005 5 mg

Resiniferatoxin-type phorboid vanilloid with capsai- cin-like selectivity for TRPV1.

LIT: Resiniferatoxin-type phorboid vanilloids display capsicain-like selectivity at native vanilloid receptors on rat DRG neurons and at the dioned vaniloid receptor VR1: A. Szallas, et al.; Br. J. Pharmacol. 128, 428 (1999). • For a comprehensive bibliography please visit our website.

PPAHV
[Phorbol 12-phenylacetate 13-acetate 20-homovanillate]

ALX-550-355-M001 1 mg
ALX-550-355-M005 5 mg

Non-opioid resiniferatoxin-type phorboid vanilloid. Agonist at rat TRPV1 (EC50 between 3 and 10µM) but virtually inactive at human TRPV1 (EC50>10µM). Induces apoptosis through a TRPV-independent mechanism.


The Resiniferatoxin Source™

High Purity High Activity Low Price

Resiniferatoxin (high purity)

[RTX]

ALX-550-179-M001 1 mg
ALX-550-179-M005 5 mg

Isolated from Euphorbia puapora. Ultrapotent capsacin analog.

LIT: For a comprehensive bibliography please visit our website.

For Bulk inquire!

Olvanil

High Quality Low Price

PAb to TRPV1

[human]

ALX-210-417-C100 100 µg


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Latest Insight

TRPC3 and TRPC6 promote neuronal survival

Transient receptor potential (TRP) channels constitute a family of cation-permeable channels with variety of physiological functions. One subfamily is formed by TRPC (canalonic) members. In a recent report, TRPC3 and TRPC6 have been shown to promote survival of cerebellar granule neurons (CGNs), by a mechanism which triggers cAMP/Ca2+-response element binding protein (CREB).


PAb to TRPC3 (CT)

PSC-3905-C100 100 µg

From rabbit. IMMUNOGEN: Synthetic peptide corresponding to 14 aa near the C-terminus of human TRPC3 (short transient receptor potential channel 3). SPECIFICITY: Recognizes human, mouse and rat TRPC3. APPLICATION: WB, BLP: PSC-3905P.

PAb to TRPC3 (NT)

PSC-3895-C100 100 µg

From rabbit. IMMUNOGEN: Synthetic peptide corresponding to 14 aa near the N-terminus of human TRPC3 (short transient receptor potential channel 3). SPECIFICITY: Recognizes human, mouse and rat TRPC3. APPLICATION: WB, BLP: PSC-3895P.

PAb to TRPC6 (CT)

PSC-3897-C100 100 µg

From rabbit. IMMUNOGEN: Synthetic peptide corresponding to 14 aa near the C-terminus of human TRPC6 (short transient receptor potential channel 6). SPECIFICITY: Recognizes human and mouse TRPC6. APPLICATION: WB, BLP: PSC-3899P.

PAb to TRPC6 (NT)

PSC-3899-C100 100 µg

From rabbit. IMMUNOGEN: Synthetic peptide corresponding to 14 aa near the N-terminus of human TRPC6 (short transient receptor potential channel 6). SPECIFICITY: Recognizes human and mouse TRPC6. APPLICATION: WB, BLP: PSC-3899P.

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TRPV1 Antagonists & Related Products

Capsazepine

**ALX-550-145-M005**
5 mg

**ALX-550-145-M025**
25 mg

Analog of capsaicin (Prod. No. ALX-550-066) that acts as a specific capsaicin antagonist.


**6'-Iodononivamide**

**ALX-550-122-M005**
5 mg

**ALX-550-122-M010**
10 mg

Potent competitive TRPV1 antagonist (IC₅₀=10nM against 100nM capsaicin; Prod. No. ALX-550-066). Convenient replacement for capsazepine (Prod. No. ALX-550-145) in most of the in vitro preparations currently used to assess the activity of putative vanilloid receptor agonist receptors.


**Isoveilleral**

**ALX-550-356-M005**
5 mg

**ALX-550-356-M001**
5 mg

**TRPV1 antagonist.**


**5'-Iodo-resiniferatoxin (I-RTX)**

**ALX-550-390-M005**
5 mg

**ALX-550-390-M001**
1 mg

**JYL-273**

**ALX-550-390-M005**
5 mg

**TRPV1 antagonist.**

LIT: For a comprehensive bibliography please visit our website.

**IBTU**

[4-(4-Chlorobenzyl)-N-4-(4-hydroxy-3-iodo-5-methoxybenzyl)thiourea]

**JY-L-1511**

**ALX-550-394-M001**
1 mg

**ALX-550-394-M005**
5 mg

Potent TRPV1 antagonist. RTX binding affinity (Kₐ=50.6nM) agonism (calcium influx EC₅₀=32.4nM) and antagonism (IC₅₀=3.37nM). For product details and chemical structure see page 7.

LIT: For a comprehensive bibliography please visit our website.

**MSK-195**

**ALX-550-396-M001**
1 mg

**ALX-550-396-M005**
5 mg

Potent analgesic with EC₅₀=0.96µg/kg in the acetic acid-induced writhing test. For product details and chemical structure see page 7.

LIT: For a comprehensive bibliography please visit our website.

**PSY-279**

**ALX-550-397-M001**
1 mg

**ALX-550-397-M005**
5 mg

**TRPV1 agonist.**

LIT: For a comprehensive bibliography please visit our website.

**Ruthenium red**

**ALX-550-295-M005**
500 mg

**ALX-550-295-G001**
1 g

Blocks TRPV1. Capsaicin and calcium antagonist. Inhibitor of Ca²⁺/Mg²⁺-ATPase.


**SB-366791**

[1-(3-Methoxyphenyl)-4-chloro-1H-pyrazole-3-carboxamide]

**ALX-550-388-M005**
1 mg

**ALX-550-388-M001**
1 mg

**JYL-827**

**ALX-550-392-M005**
5 mg

**ALX-550-392-M001**
1 mg

**TRPV1 agonist.**

LIT: For a comprehensive bibliography please visit our website.

**JYL-1413**

**ALX-550-392-M005**
1 mg

**JYL-273**

**ALX-550-390-M005**
5 mg

**TRPV1 antagonist.**

LIT: For a comprehensive bibliography please visit our website.

**JYL-1511**

**ALX-550-394-M001**
1 mg

**ALX-550-394-M005**
5 mg

Potent TRPV1 antagonist. RTX binding affinity (Kₐ=50.6nM) agonism (calcium influx EC₅₀=32.4nM) and antagonism (IC₅₀=3.37nM). For product details and chemical structure see page 7.

LIT: For a comprehensive bibliography please visit our website.

**SU-154**

**ALX-550-395-M001**
1 mg

**ALX-550-395-M005**
5 mg

**TRPV1 agonist.**

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After the identification of resiniferatoxin (RTX) as a archetypal vanilloid receptor TRPV1 agonist with a binding potency approximately 4 orders of magnitude greater than that of capsaicin (CAP) (RTX: Kᵢ = 0.13 nM, CAP: Kᵢ = 1.700 nM in CHO/TRPV1 [1]), and on the basis of previously published SAR studies on RTX [2], Jeewoo Lee et al. proposed a hypothetical pharmacophore model for the interaction with the capsaicin binding site of TRPV1 in which four groups, 4-hydroxy-3-methoxyphenyl (A-region), C₂-ester (B-region), orthophenyl (C₁-region) and C₃-keto (C₂-region) represent principal pharmacophores (see Figure 2). On the basis of this model, two ultrapotent TRPV1 agonists, JYL-79 and JYL-273, with Kᵢ values of 19 nM and 11 nM, respectively, in a [³H]RTX binding assay, have been synthesized and characterized [3, 4]. Relative to capsaicin these compounds appear to be approximately 300 and 500 times more potent.

A similar compound is N′-(4-tert-butylbenzyl)-N-3-methoxy-4-(methylsulfonfonylamino)benzyl-thiourea (JYL-1511) [6].

In the SAR of the A-region, JYL-1433 (the 3-fluoro analog of JYL-827) was a full and potent TRPV1 antagonist with an IC₅₀ = 7.8 nM [5].

In the SAR of the B-region, compounds with potent analgesic activity were found. Despite its relatively weak in vitro potency, SU-154, an Nc-hydroxy thiourea analog, exhibited high analog potencies in the acetic writhing assay [7].

Among a series of derivatives in which the distances between the proposed four pharmacophores in the lead compound JYL-827 have been varied, the JYL-1413 has shown to be a TRPV1 antagonist with an IC₅₀ = 7.8 nM [5].

Another amide based RTX analog, N-[2-(4-tert-butylbenzyl)-3-(pivaloyloxy)propyl]-N′-(4-hydroxy-3-methoxyphenyl)acetamide (PSY-279) approaches the high agonism of RTX in the CHO/TRPV1 cells (RTX: EC₅₀ = 0.27 nM, PSY-279: EC₅₀ = 0.29 nM) [4, 9].

Finally two other high affinity TRPV1 receptor agonists were synthesized and characterized by the group including Jeewoo Lee, MK056 (KJM-429) and SC0030 (JYL-1421) [10-12].

The isosteric replacement of the phenolic hydroxyl groups in the potent TRPV1 agonists JYL-79 and JYL-273 with the alkylsulfonamido group provided a series of compounds which are effective antagonists to the action of capsaicin on rat TRPV1 [5]. As a prototype, N-[2-(3,4-dimethylbenzyl)-3-pivaloyloxypropyl]-N′-[4-(methylsulfonfonyl)benzyl]thiourea (JYL-827) showed a high binding affinity with a Ki value of 29.3 nM for the inhibition of [³H]RTX binding and potent antagonism with an IC₅₀ value of 67 nM for the inhibition of Ca²⁺ uptake in response to capsaicin, displaying partial agonism [6]. The SAR of the prototype has been examined extensively based on the pharmacophoric regions represented in Figure 2 [5, 7].

A similar compound is N′-(4-tert-butylbenzyl)-N-3-methoxy-4-(methylsulfonfonyl)benzyl-thiourea (JYL-1511) [6].

In the SAR of the A-region, JYL-1433 (the 3-fluoro analog of JYL-827) was a full and potent TRPV1 antagonist with an IC₅₀ = 7.8 nM [5].

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Finally two other high affinity TRPV1 receptor agonists were synthesized and characterized by the group including Jeewoo Lee, MK056 (KJM-429) and SC0030 (JYL-1421) [10-12].

The related compound N-[2-(3,4-dimethylbenzyl)-3-(pivaloyloxy)propyl]-2-(4-(2-aminothoxy)-3-methoxyphenyl)acetamide (MSK-195) is a potent analgesic with an EC₅₀ = 0.96 µg/kg in the acetic acid-induced writhing test [4].
**TRPV1 Modulation**

**Adenosine 5'-triphosphate . 2Na**

- ALX-480-021-G001
  - 1 g
- ALX-480-021-G005
  - 5 g

**Bradykinin**

- ALX-152-006-M005
  - 5 mg
- ALX-152-006-M025
  - 25 mg

**For a comprehensive bibliography please visit our website.**

**MAB to Bradykinin (MBK3)**

- ALX-804-647-R100
  - 100 µg
- CLONE: MBK3, ISO TYPE: Mouse IgG1.
- IMMUNOGEN: Bradykinin.
- SPECIFICITY: Recognizes Bradykinin from various species. APPLICATION: WB.
- LIT: For a comprehensive bibliography please visit our website.

**PAB to Bradykinin B₂ Receptor**

- ALX-210-872-R200
  - 200 µg

**PAB to Prokineticin Receptor 1 (human) (NT)**

- CVL-PAB0192-1
  - 200 µg

**MAB to TRK Receptor (human) (MGR12)**

- ALX-804-575-C100
  - 100 µg
- CLONE: MGR12, ISO TYPE: Mouse IgG1.
- IMMUNOGEN: SK-N-BE neuroblastoma cell line transfected with TrkA (TRK receptor).
- SPECIFICITY: Recognizes an epitope present in the extracellular domain of human TrkA. Detects a band of ~140kDa by IP. APPLICATION: FC, IHC (PS), WB, FACS.
- LIT: For a comprehensive bibliography please visit our website.

**Prostaglandin E₂**

- ALX-340-028-M001
  - 1 mg
- ALX-340-028-M010
  - 10 mg

**Serotonin . HCl**

- ALX-340-528-M050
  - 50 µg
- ALX-340-528-M250
  - 250 µg
- ALX-340-528-G001
  - 1 g

**For a comprehensive bibliography please visit our website.**

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**TRPV4 & Related Products**

The relevance of anandamide as an endovanilloid is further highlighted by its identification as an endogenous activator of TRPV4 (OCTRCP-C; VRL-2; VR-OAC; TRP12) [1–4], an observation which adds to the growing receptor promiscuity of this important endogenous lipid. The activation of TRPV4 by anandamide is indirect and mediated by oxidative metabolites of arachidonic acid. TRPV4 was originally characterised as an osmotically regulated ion channel sensing changes in cell volume, but was later discovered to be activated not only by physical stimuli, such as cell swelling or heat. It is basically a thermosensor similar to TRPV1 but insensitive to capsaicin. TRPV4 is activated under physiological conditions by non-tumor promoter phorbol 4-cholesterol decanoate (4c-PCDD) [2]. 4c-PCDD does not activate TRPV1 like phorbol 12,13-didecanoate (PDDDH), another resinsiferatoxin-type vanilloid. TRPV4 is an interesting new pharmacological target whose potential is just beginning to surface.

**FRPV4 Agonist**

**5'-Epoxycaprostane acid**

- ALX-340-059-G025
  - 25 µg
- ALX-340-059-G050
  - 50 µg

**Endogenous TRPV4 agonist (K=150nM).**


**TRPV4 Activator**

**4c-Phorbol 12,13-didecanoate**

- ALX-445-006-M001
  - 1 mg
- ALX-445-006-M010
  - 5 mg

**Activator of TRPV4. Negative control for phorbol 12,13-didecanoate (PDD) (Prod. No. ALX-404-002).**


**For a comprehensive bibliography please visit our website.**

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**TRPM8 [CMR1]/TRPA1 Activator**

**NEW Icillin**

- ALX-420-037-M001
  - 1 mg
- ALX-420-037-M005
  - 5 mg
- ALX-420-037-M025
  - 25 mg

**Cooling agent. Strongly activates TRPM8 (cold menthol receptor 1 (CMR1) and TRPA1 at 10- to 100-fold higher concentration).**

**For a comprehensive bibliography please visit our website.**

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**Coming Soon!**

**WS-12 – An Ultra Potent TRPM8 Agonist**

B. Beck, et al. recently described the new compound WS-12 as the highest-affinity TRPM8 (transient receptor potential melatonin B) ligand known to date, with an EC₅₀ value about 2000 times lower than that of menthol.


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**For a comprehensive bibliography please visit our website.**

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