ALEXIS® BIOCHEMICALS

TOPIX Special Edition

FOCUS NEUROSCIENCE

International Edition

June 2006

Contents

ALEXIS® BIOCHEMICALS

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Cannabinoid Research Tools

see Page 3 – 5

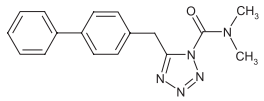
NEW Potent Inhibitor of Anandamide Uptake

NEW **LY2183240**

ALX-550-411-M010 10 mg
ALX-550-411-M050 50 mg

Potent, competitive small molecule inhibitor of anandamide uptake (IC_{50}=270 ± 29.4pM) to characterize a high-affinity, saturable anandamide transporter binding site that is distinct from fatty acid amide hydrolase (FAAH).

LIT: Identification of a high-affinity binding site involved in the transport of endocannabinoids: S.A. Moore, et al.; PNAS **102,** 17852 (2005) ▪ Commented in: Toward an anandamide transporter: R. Mechoulam and D.G. Deutsch; PNAS **102,** 17541 (2005)



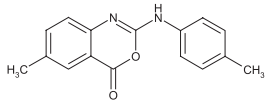
NEW Non-Competitive Inhibitor of MGL

NEW **URB754** BULK

ALX-550-410-M001 1 mg
ALX-550-410-M005 5 mg

Potent, noncompetitive inhibitor of monoacyl-glycerol lipase (MGL), which hydrolyzes 2-arachidonoylglycerol (2-AG) to arachidonic acid and glycerol. IC_{50}=200nM for the recombinant rat brain enzyme. Inhibits rat brain fatty acid amide hydrolase (FAAH) less effectively (IC_{50}=32μM) and binds weakly to the rat CB_1 receptor (IC_{50}=3.8μM).

LIT: Selective inhibition of 2-AG hydrolysis enhances endocannabinoid signaling in hippocampus: J. K. Makara, et al.; Nat. Neurosci. **8,** 1139 (2005)



NEW Tool for HTS

NEW

Angiotensin-converting Enzyme 2 [ACE2]

ACE2 (human):Fc (human) (rec.) BULK
ALX-201-330-C050 50 μg

MAb to ACE2 (human) (AC18F)
ALX-804-715-C050 50 μg

For more information please see Page 13!

Latest Additions to Dependence Receptors

Netrin-1 (human) (rec.)
ALX-522-100-2010 2 x 10 μg

UNC5B (human):Fc (human) (rec.)
ALX-522-095-C050 50 μg

MAb to Netrin-1 (human) (Nora-1)
ALX-804-838-C100 100 μg

RGMA, Soluble (human) (rec.)
ALX-522-103-2010 2 x 10 μg

RGMC, Soluble (human) (rec.)
ALX-522-104-C010 10 μg

For more information please see Page 9!

Comprehensive Panel of Gangliosides & Sphingolipids

see Page 9

New Metabotropic Glutamate Receptor Modulators

see Page 10

ALEXIS® BIOCHEMICALS

BIOMOL

The Receptor Connection

offering a daily increasing number of G Protein Coupled Receptors [GPCRs]

MRP*grade*™ Receptors

Product No.	Product Name	Size	
BXT-C101920-4	Adenosine Receptor A_1 (human) (MRP*grade*™)	4x50 Units	
BXT-C102020-4	Adenosine Receptor A_{2a} (human) (MRP*grade*™)	4x50 Units	
BXT-C102120-4	Adenosine Receptor A_{2b} (human) (MRP*grade*™)	4x50 Units	
BXT-C101420-4	Adrenergic Receptor α_1A (rat) (MRP*grade*™)	4x50 Units	
BXT-C101520-4	Adrenergic Receptor α_1B (human) (MRP*grade*™)	4x50 Units	
BXT-C110520-4	Adrenergic Receptor α_1B (mesau) (MRP*grade*™)	4x50 Units	
BXT-C101620-4	Adrenergic Receptor α_2B (human) (MRP*grade*™)	4x50 Units	
BXT-C101820-4	Adrenergic Receptor α_2C (rat) (MRP*grade*™)	4x50 Units	
BXT-C103320-4	Bradykinin Receptor B_2 (human) (MRP*grade*™)	4x50 Units	
BXT-C103620-4	Cannabinoid Receptor 1 (human) (MRP*grade*™)	4x50 Units	
BXT-C103720-4	Cannabinoid Receptor 2 (human) (MRP*grade*™)	4x50 Units	
BXT-C112120-4	Cannabinoid Receptor 1 (mouse) (MRP*grade*™)	4x50 Units	
BXT-C216320-4	CXCR4 (human) (MRP*grade*™)	4x50 Units	
BXT-C110920-4	Dopamine Receptor D_{1A} (human) (MRP*grade*™)	4x50 Units	
BXT-C104320-4	Dopamine Receptor D_2 (human) (MRP*grade*™)	4x50 Units	
BXT-C104420-4	Dopamine Receptor D_2 (mouse) (MRP*grade*™)	4x50 Units	
BXT-C104520-4	Dopamine Receptor D_3 (human) (MRP*grade*™)	4x50 Units	
BXT-C104620-4	Dopamine Receptor D_4 (human) (MRP*grade*™)	4x50 Units	
BXT-C105420-4	Galanin Receptor Type 1 (human) (MRP*grade*™)	4x50 Units	
BXT-C105620-4	Galanin Receptor Type 3 (human) (MRP*grade*™)	4x50 Units	
BXT-C106120-4	Histamine Receptor H_2 (human) (MRP*grade*™)	4x50 Units	
BXT-C106220-4	Histamine Receptor H_2 (rat) (MRP*grade*™)	4x50 Units	
BXT-C106820-4	Metabotropic Glutamate Receptor 3 (human) (MRP*grade*™)	4x50 Units	
BXT-C111420-4	Metabotropic Glutamate Receptor 7 (human) (MRP*grade*™)	4x50 Units	
BXT-C102320-4	Muscarinic Acetylcholine Receptor M_1 (human) (MRP*grade*™)	4x50 Units	
BXT-C102420-4	Muscarinic Acetylcholine Receptor M_1 (mouse) (MRP*grade*™)	4x50 Units	
BXT-C102520-4	Muscarinic Acetylcholine Receptor M_2 (human) (MRP*grade*™)	4x50 Units	
BXT-C102620-4	Muscarinic Acetylcholine Receptor M_2 (pig) (MRP*grade*™)	4x50 Units	
BXT-C107220-4	Substance P Receptor (human) (MRP*grade*™)	4x50 Units	
BXT-C107320-4	Substance P Receptor (rat) (MRP*grade*™)	4x50 Units	
BXT-C107420-4	Substance K Receptor (human) (MRP*grade*™)	4x50 Units	
BXT-C107520-4	Substance K Receptor (rat) (MRP*grade*™)	4x50 Units	
BXT-C107620-4	Neuromedin K Receptor (human) (MRP*grade*™)	4x50 Units	
BXT-C108420-4	Opioid Receptor δ (mouse) (MRP*grade*™)	4x50 Units	
BXT-C108520-4	Opioid Receptor κ (human) (MRP*grade*™)	4x50 Units	
BXT-C108620-4	Opioid Receptor κ (mouse) (MRP*grade*™)	4x50 Units	
BXT-C100120-4	Serotonin Receptor 1A [5-HT1A] (human) (MRP*grade*™)	4x50 Units	
BXT-C100220-4	Serotonin Receptor 1B [5-HT1B] (human) (MRP*grade*™)	4x50 Units	
BXT-C100320-4	Serotonin Receptor 1D [5-HT1D] (human) (MRP*grade*™)	4x50 Units	
BXT-C100420-4	Serotonin Receptor 1E [5-HT1E] (human) (MRP*grade*™)	4x50 Units	
BXT-C100520-4	Serotonin Receptor 1F [5-HT1F] (human) (MRP*grade*™)	4x50 Units	
BXT-C100620-4	Serotonin Receptor 2A [5-HT2A] (human) (MRP*grade*™)	4x50 Units	
BXT-C101020-4	Serotonin Receptor 5A [5-HT5A] (human) (MRP*grade*™)	4x50 Units	
BXT-C111120-4	Serotonin Receptor 6 [5-HT6] (rat) (MRP*grade*™)	4x50 Units	
BXT-C111720-4	Serotonin Receptor 7 [5-HT7] (rat) (MRP*grade*™)	4x50 Units	
BXT-C109320-4	Somatostatin Receptor Type 1 (human) (MRP*grade*™)	4x50 Units	
BXT-C109420-4	Somatostatin Receptor Type 2 (human) (MRP*grade*™)	4x50 Units	
BXT-C109520-4	Somatostatin Receptor Type 3 (human) (MRP*grade*™)	4x50 Units	

MRP*grade*™ Receptors (continued)

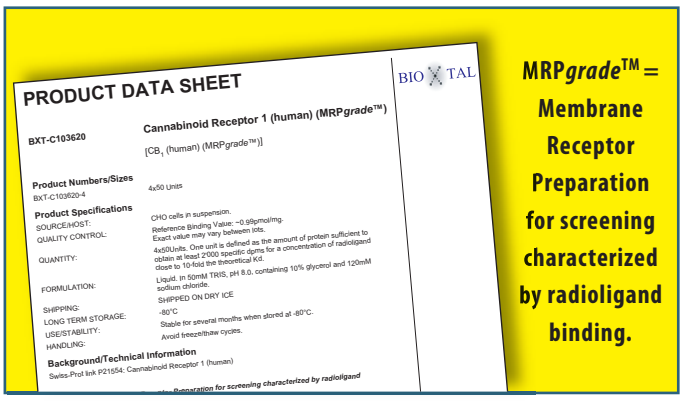
Product No.	Product Name	Size	
BXT-C107220-4	Substance P Receptor (human) (MRP*grade*™)	4x50 Units	
BXT-C107320-4	Substance P Receptor (rat) (MRP*grade*™)	4x50 Units	
BXT-C107420-4	Substance K Receptor (human) (MRP*grade*™)	4x50 Units	
BXT-C107520-4	Substance K Receptor (rat) (MRP*grade*™)	4x50 Units	
BXT-C216320-4	Vasopressin Receptor 1a (human) (MRP*grade*™)	4x50 Units	
BXT-C110320-4	Vasopressin Receptor 1b (human) (MRP*grade*™)	4x50 Units	

Membrane Preparations of Orphan Receptors

Product No.	Product Name	Size	
BXT-N105920-5	Glucagon Receptor (human)	5x1mg	
BXT-N113320-5	Lutropin-choriogonadotropic Hormone Receptor (rat)	5x1mg	
BXT-N214020-5	Probable P2Y Purinoceptor GPR17 (human)	5x1mg	
BXT-N109020-5	Prostaglandin E_2 Receptor EP3 (human)	5x1mg	
BXT-N108920-5	Purinergic Receptor P2Y1 (human)	5x1mg	
BXT-N108720-5	Purinergic Receptor P2Y2 (human)	5x1mg	
BXT-N104820-5	Sphingosine 1-phosphate Receptor (human)	5x1mg	
BXT-N111620-5	Thyrotropin Receptor (rat)	5x1mg	

In Development

Product No.	Product Name
BXT-C110720-4	Adrenergic Receptor α_2A (human) (MRP*grade*™)
BXT-C111020-4	Dopamine Receptor D1B (human) (MRP*grade*™)
BXT-C108120-4	Neuropeptide Receptor NPY4 (human) (MRP*grade*™)
BXT-C108320-4	Opioid Receptor δ (human) (MRP*grade*™)
BXT-C100720-4	Serotonin Receptor 2A [5-HT2A] (mouse) (MRP*grade*™)
BXT-C100820-4	Serotonin Receptor 2B [5-HT2B] (human) (MRP*grade*™)
BXT-C100920-4	Serotonin Receptor 2C [5-HT2C] (human)) (MRP*grade*™)
BXT-C101220-4	Serotonin Receptor 7 [5-HT7] (human) (MRP*grade*™)
BXT-C216320-4	Vasopressin Receptor V2 (human) (MRP*grade*™)



MRP*grade*™ = Membrane Receptor Preparation for screening characterized by radioligand binding.

ALEXIS® BIOCHEMICALS

Leading the Cannabinoid Receptor & Vanilloid Receptor [TRPV1] Research

The TRP (Transient Receptor Potential) Superfamily

TRPV4

The relevance of anandamide as an endovanilloid is further highlighted by its identification as an endogenous activator of TRPV4 (OTRPC4; 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 the non-tumor promoter phorboid 4α-phorbol didecanoate (4α-PDD) [2]. 4α-PDD does not activate TRPV1 like phorbol 12,13-didecanoate 20-homovanillate (PDDHV) (Prod. No. ALX-550-371), another resiniferatoxin-type phorboid vanilloid. TRPV4 is an interesting new pharmacological target whose potential is just beginning to surface.

LIT: [1] Anandamide and arachidonic acid use epoxyeicosatrienoic acids to activate TRPV4 channels: H. Watanabe, et al.; Nature **424,** 434 (2003) ▪ **[2]** Activation of TRPV4 channels (hVRL-2/mTRP12) by phorbol derivatives: H. Watanabe, et al.; J. Biol. Chem. **277,** 13569 (2002) ▪ **[3]** The TRPV4 channel: structure-function relationship and promiscuous gating behaviour: B. Nilius, et al.; Pflugers Arch. **446,** 298 (2003) ▪ **[4]** TRPV4 calcium entry channel: a paradigm for gating diversity: B. Nilius, et al.; Am. J. Physiol. Cell Physiol. **286,** C195 (2004)

TRPV4 Agonist

5',6'-Epoxyeicosatrienoic acid

ALX-340-059-C025	25 µg
ALX-340-059-C050	50 µg

Endogenous TRPV4 agonist (K_i=150nM).

LIT: Anandamide and arachidonic acid use epoxyeicosatrienoic acids to activate TRPV4 channels: H. Watanabe, et al.; Nature **424,** 434 (2003)

TRPV4 Activator

4α-Phorbol 12,13-didecanoate BULK

ALX-445-006-M001	1 mg
ALX-445-006-M005	5 mg

Activator of TRPV4. Negative control for phorbol 12,13-didecanoate (PDD) (Prod. No. ALX-445-002).

LIT: Activation of TRPV4 channels (hVRL-2/mTRP12) by phorbol derivatives: H. Watanabe, et al.; J. Biol. Chem. **277,** 13569 (2002) ▪ TRPV4 calcium entry channel: a paradigm for gating diversity: B. Nilius, et al.; Am. J. Physiol. Cell Physiol. **286,** C195 (2004)

For updated prices please visit

www.axxora.com

Antibody to TRPV1

PAb to TRPV1 (human)

ALX-210-417-C100	100 µg

From rabbit. **IMMUNOGEN:** Synthetic peptide corresponding to aa 7-21 (T^7DLGAAADPLQK-DTC^{21}) of human vanilloid receptor 1 (TRPV1). **SPECIFICITY:** Recognizes human TRPV1. **APPLICATION:** IHC (FS), ICC.

LIT: Deletion of vanilloid receptor 1-expressing primary afferent neurons for pain control: L. Karai, et al.; J. Clin. Invest. **113,** 1344 (2004)

Activator of TRPV1, V2 & V3

2-Aminoethoxydiphenyl borate

ALX-400-045-M100	100 mg

Cell permeable modulator of Ins(1,4,5)-P_3-induced Ca^{2+} release. A prototype drug for a group of structurally related calcium channel blockers in human platelets. Has been shown, in the absence of other stimuli, to activate TRPV1, V2 and V3, but not TRPV4, V5 and V6 expressed in HEK293 cells.

LIT: 2APB, 2-aminoethoxydiphenyl borate, a membrane-penetrable modulator of Ins(1,4,5)P3-induced Ca2+ release: T. Maruyama, et al.; J. Biochem. **122,** 498 (1997)

Potent TRPV1 Antagonist

SB366791 BULK

ALX-550-388-M001	1 mg
ALX-550-388-M005	5 mg
ALX-550-388-M025	25 mg

Potent and selective TRPV1 antagonist.

LIT: Identification of SB-366791, a potent and selective antagonist of vanilloid receptor-1: H.K. Rami, et al.; Drugs Fut. **27** (Supply A), 411 (2002) ▪ Identification and charakterisation of SB-366791, a potent and selective vanilloid receptor (VR1/TRPV1) antagonist: M.J. Gunthorpe, et al.; Neuropharmacology **46,** 133 (2004) ▪ Effects of the novel TRPV1 receptor antagonist SB366791 in vitro and in vivo in the rat: A. Varga, et al.; Neurosci. Lett. **385,** 137 (2005)

SU-154

ALX-550-395-M001	1 mg
ALX-550-395-M005	5 mg

TRPV1 antagonist. Nc-hydroxy thiourea analog with high analgesic potency in the acetic writhing assay. RTX binding affinity (K_i=212nM), antagonism (IC_{50}=94nM).

LIT: Analysis of structure-activity relationships for the ‚B-region' of N-(3-acyloxy-2-benzylpropyl)-N(,)-[4-(methylsulfonylamino)benzyl]thiourea analogues as vanilloid receptor antagonists: discovery of an N-hydroxythiourea analogue with po: J. Lee, et al.; Bioorg. Med. Chem. Lett. **14,** 2291 (2004)

TRPM8 [CMR1]/TRPA1 Activator

NEW Icilin [AG-3-5] BULK

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

Cooling agent. Strongly activates TRPM8 (cold methanol receptor 1 (CMR1)) and TRPA1 (at 10- to 100-fold higher concentration). Induces currents in TRPM8 expressing HEK 293 cells (EC_{50}=0.36mM) more potently than menthol or low temperatures.

LIT: AG-3-5: a chemical producing sensations of cold: E.T. Wei and D.A. Seid; J. Pharm. Pharmacol. **35,** 110 (1983) ▪ TRPM8 activation by menthol, icilin, and cold is differentially modulated by intracellular pH: D.A. Andersson, et al.; J. Neurosci. **24,** 5364 (2004)

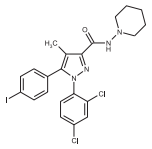
Cannabinoid Receptors Modulators

AM 251

ALX-270-239-M001	1 mg
ALX-270-239-M005	5 mg

Structurally related to the cannabinoid receptor (CB) antagonist SR 141716A. Binds with high affinity to cannabinoid receptor CB_1 (K_i=7.49nM; 306-fold selective over CB_2 receptors).

LIT: Binding of the non-classical cannabinoid CP 55, 940, and the diarylpyrazole AM251 to rodent brain cannabinoid receptors: S.J. Gatley, et al.; Life Sci. **61,** PL 191 (1997) ▪ Structure-activity relationships of pyrazole derivatives as cannabinoid receptor antagonists: R. Lan, et al.; J. Med. Chem. **42,** 769 (1999)



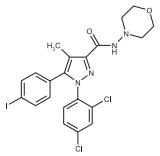
AM 251

AM 281

ALX-270-240-M001	1 mg
ALX-270-240-M005	5 mg

Analog of the cannabinoid receptor (CB) antagonist SR 141716A. Potent CB_1 receptor antagonist/inverse agonist (K_i=14nM).

LIT: Effect of the cannabinoid receptor SPECT agent, AM 281, on hippocampal acetylcholine release from rat brain slices: A.N. Gifford, et al.; Neurosci. Lett. **238,** 84 (1997)



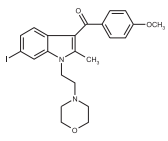
AM 281

AM 630 BULK

ALX-270-241-M001	1 mg
ALX-270-241-M005	5 mg

Competitive CB_1 receptor antagonist in guinea-pig brain. Shows also agonist properties. CB_2 antagonist/inverse agonist (K_i=31.2nM; 165-fold selective over CB_1 receptors).

LIT: AM630, a competitive cannabinoid receptor antagonist: R. Pertwee, et al.; Life Sci. **56,** 1949 (1995)



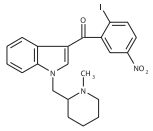
AM 630

AM 1241 BULK

ALX-550-383-M001	1 mg
ALX-550-383-M005	5 mg

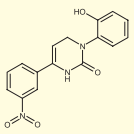
Potent and selective CB_2 receptor agonist (K_i=3.4nM (mouse), K_i=280nM (rat)) also *in vivo.*

LIT: CB2 cannabinoid receptor-mediated peripheral antinociception: T.P. Malan, Jr., et al.; Pain **93,** 239 (2001) ▪ Activation of CB2 cannabinoid receptors by AM1241 inhibits experimental neuropathic pain: pain inhibition by receptors not present in the CNS: M.M. Ibrahim, et al.; PNAS **100,** 10529 (2003)

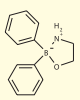


AM 1241

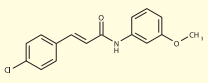
Chemical Structures



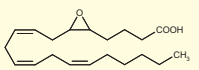
Icilin



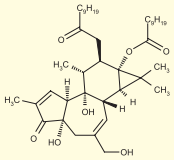
2-Aminoethoxy-diphenyl borate



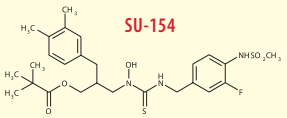
SB366791



5',6'-Epoxyeicosatrienoic acid



4α-Phorbol 12,13-didecanoate



SU-154

Purified (PF) = Purified (Preservative free); FC = Flow Cytometry; ICC = Immunocytochemistry; IP = Immunoprecipitation; IHC = Immunohistochemistry (FS = Frozen Sections, PS = Paraffin Sections); WB = Western blot; BP = Blocking Peptide

Cannabinoid Receptors Antibodies

PAb to Cannabinoid Receptor 1
ALX-210-316-R100 100 µl

From rabbit. **IMMUNOGEN:** Recombinant rat CB_1 (cannabinoid receptor 1) fusion protein (aa 1-77). **SPECIFICITY:** Recognizes human, non-human primate, mouse, rat, amphibian, chicken and fish CB_1. Detects a band of ~60kDa by Western blot representing CB_1; also detects less intense bands of ~23kDa, ~72kDa and ~180kDa from rat brain homogenate. **APPLICATION:** IHC (PS), ICC, WB.

PAb to Cannabinoid Receptor 1
ALX-210-314-R100 100 µl

From rabbit. **IMMUNOGEN:** Recombinant human CB_1 (cannabinoid receptor 1) fusion protein (aa 1-99). **SPECIFICITY:** Recognizes human and rat CB_1. Detects a band of ~60kDa by Western blot. **APPLICATION:** IHC (FS, PS), ICC, WB.

PAb to Cannabinoid Receptor 2
ALX-210-317-R100 100 µl

From rabbit. **IMMUNOGEN:** Recombinant rat CB_2 (cannabinoid receptor 2) fusion protein (aa 1-32). **SPECIFICITY:** Recognizes human and rat CB_2. **APPLICATION:** ICC.

PAb to Cannabinoid Receptor 2
ALX-210-198-1 1 Vial

From rabbit. **IMMUNOGEN:** Synthetic peptide corresponding to aa 20-33 (N^{20}PMKDYMILSGPQK^{33}) of N-terminal human CB_2 (cannabinoid receptor 2). **SPECIFICITY:** Recognizes human and mouse CB_2. Detects a band of ~45kDa by Western blot. Does not cross-react with CB_1. **APPLICATION:** IHC (PS), WB.

LIT: Inhibition of skin tumor growth and angiogenesis in vivo by activation of cannabinoid receptors: M.L. Casanova, et al.; J. Clin. Invest. **111,** 43 (2003)

PAb to Cannabinoid Receptor 2 (human)
ALX-210-315-R100 100 µl

From rabbit. **IMMUNOGEN:** Recombinant human CB_2 (cannabinoid receptor 2) fusion protein (aa 1-33). **SPECIFICITY:** Recognizes human CB_2. Detects a band of ~60kDa by Western blot. **APPLICATION:** FC, IHC (FS, PS), ICC, WB.

LIT: Distinct expression profiles of the peripheral cannabinoid receptor in lymphoid tissues depending on receptor activation status: N. Rayman, et al.; J. Immunol. **172,** 2111 (2004) ▪ The peripheral cannabinoid receptor Cb2, frequently expressed on AML blasts, either induces a neutrophilic differentiation block or confers abnormal migration properties in a ligand-dependent manner: M. Alberich Jorda, et al.; Blood **104,** 526 (2004)

Cannabinoid Receptors

Cannabinoid Receptor 1 (human) (MRP*grade*™)
BXT-C103620-4 4 x 50 Units

CHO cells in suspension.

Cannabinoid Receptor 2 (human) (MRP*grade*™)
BXT-C103720-4 4 x 50 Units

BHK cells in suspension.

Latest Insight

H.A. Overton, et al. described the endogenous lipid signalling agent oleoylethanolamide (OEA) as a peripherally acting agent that reduces food intake and body weight gain in rat feeding models. Recently, evidence was shown that OEA is an endogenous ligand of the orphan receptor GPR119, a G protein coupled receptor (GPCR) expressed predominantly in the human and rodent pancreas and gastrointestinal tract and also in rodent brain, suggesting that the reported effects of OEA on food intake may be mediated, at least in part, via the GPR119 receptor.

LIT: Deorphanization of a G protein-coupled receptor for oleoylethanolamide and its use in the discovery of small-molecule hypophagic agents: H.A. Overton, et al.; Cell Metab. **3,** 167 (2006)

For Oleoylethanolamide [OEA] see Page 5

Endocannabinoids

Anandamide BULK
ALX-340-029-M005 5 mg

Endogenous ligand for the CB_1 receptor (CB_1: K_i=52nm; CB_2: K_i=1930nm) and TRPV1 (K_i=5.78µM). Inhibits NF-κB activation through direct binding to IKKβ and induces apoptosis independently of cannabinoid or vanilloid receptors. Activates the MAP kinase (MAPK/ERK) signalling pathway

LIT: Isolation and structure of a brain constituent that binds to the cannabinoid receptor: W.A. Devane, et al.; Science **258,** 1946 (1992)

Selected Review Articles
Anandamide transport: M.J. McFarland & E.L. Barker; Pharmacol. Ther. **104,** 117 (2004) ▪ Anandamide as an intracellular messenger regulating ion channel activity: M. van der Stelt & V. Di Marzo; Prostaglandins Other Lipid Mediat. **77,** 111 (2005)

N-Arachidonoyldopamine
[NADA]

ALX-340-049-M001 1 mg
ALX-340-049-M005 5 mg

Endogenous, specific ligand for the CB_1 receptor (CB_1: K_i=250nM; CB_2: K_i=12µM) and TRPV1 (EC_{50}=50nM) found in nervous tissues [3, 4]. Immunosuppressant inhibiting T cell proliferation and phosphorylation of the NF-κB p65 subunit. Potent vasorelaxant and inhibitor of HIV-1.

LIT: N-acyl-dopamines: novel synthetic CB(1) cannabinoid-receptor ligands and inhibitors of anandamide inactivation with cannabimimetic activity in vitro and in vivo: T. Bisogno, et al.; Biochem. J. **351,** 817 (2000) ▪ Synthesis and biological evaluation of novel amides of polyunsaturated fatty acids with dopamine: V. Bezuglov, et al.; Bioorg. Med. Chem. Lett. **11,** 447 (2001)

2-Arachidonoylglycerol
ALX-340-036-M005 5 mg

Endogenous ligand for the CB_1 receptor (CB_1: K_i=58.3nM); CB_2: K_i>3µM) present in high levels in the CNS.

LIT: A second endogenous cannabinoid that modulates long-term potentiation: N. Stella, et al.; Nature **388,** 773 (1997)

Noladin ether
ALX-340-052-M005 5 mg

Endogenous specific ligand for the CB_1 and CB_2 receptor. Chemically stable, but less potent than 2-arachidonoylglycerol (Prod. No. ALX-340-036) with an endogenous half-life time of hours rather than minutes.

LIT: 2-arachidonyl glyceryl ether, an endogenous agonist of the cannabinoid CB1 receptor: L. Hanus, et al.; PNAS **98,** 3662 (2001)

cis-9,10-Octadecenamide
[Oleamide, ODA]

ALX-550-121-M010 10 mg

Sleep-inducing brain lipid. Shown to be a full CB_1 but not CB_2 receptor agonist.

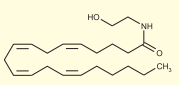
LIT: Chemical characterization of a family of brain lipids that induce sleep: B.F. Cravatt, et al.; Science **268,** 1506 (1995) ▪ Oleamide is a selective endogenous agonist of rat and human CB1 cannabinoid receptors: J.D. Leggett, et al.; Br. J. Pharmacol. **141,** 253 (2004)

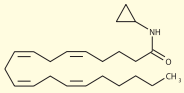
Virodhamine . HCl
ALX-340-051-M005 5 mg

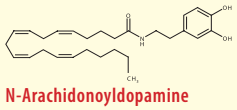
Endogenous endocannabinoid. Partial agonist with *in vivo* antagonist activity at the CB_1 receptor (EC_{50}=1.9µM; 61% efficacy), full agonist for the CB_2 receptor (100% efficacy).

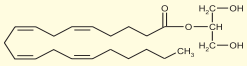
LIT: Characterization of a novel endocannabinoid, virodhamine, with antagonist activity at the CB1 receptor: A.C. Porter, et al.; J. Pharmacol. Exp. Ther. **301,** 1020 (2002)

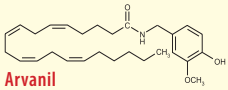
Chemical Structures

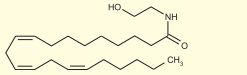

Anandamide

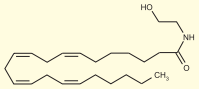

Arachidonoyl cyclopropylamide

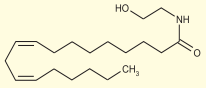

N-Arachidonoyldopamine

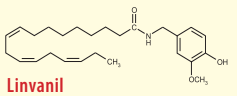

2-Arachidonoylglycerol

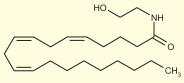

Arvanil

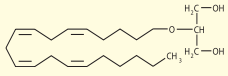

Dihomo-γ-linolenylethanolamide

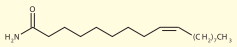

Docosatetraenylethanolamide

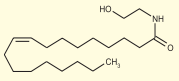

Linoleylethanolamide

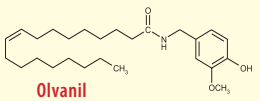

Linvanil

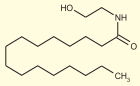

Mead acid ethanolamide

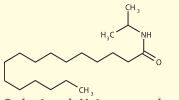

Noladin ether

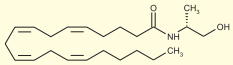

cis-9,10-Octadecenamide

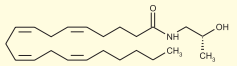

Oleoylethanolamide

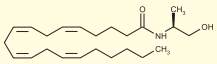

Olvanil

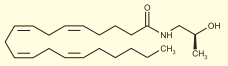

Palmitoylethanolamide

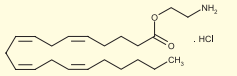

Palmitoyl-N-isopropylamide


R-1 Methanandamide


R-2 Methanandamide


S-1 Methanandamide


S-2 Methanandamide


Virodhamine . HCl

Anandamide Related Products

N-Arachidonoyl-γ-aminobutyric acid
ALX-340-050-M005 5 mg

Arachidonoyl 2'-chloroethylamide
ALX-340-053-M005 5 mg

Arachidonoyl cyclopropylamide
ALX-340-054-M005 5 mg

Potent and selective CB_1 agonist (K_i=2.2nM). Displays 325-fold selectivity over CB_2 receptors (K_i=0.7μM). Active *in vivo.*

LIT: Synthesis and characterization of potent and selective agonists of the neuronal cannabinoid receptor (CB1): C.J. Hillard, et al.; J. Pharmacol. Exp. Ther. **289,** 1427 (1999) ▪ Arachidonylcyclopropylamide increases microglial cell migration through cannabinoid CB2 and abnormal-cannabidiol-sensitive receptors: A. Franklin, et al.; Eur. J. Pharmacol. **474,** 195 (2003) ▪ The interaction of cannabinoids and opioids on pentylenetetrazole-induced seizure threshold in mice: H. Shafaroodi, et al.; Neuropharmacology **47,** 390 (2004)

Arachidonoyl 2'-fluoroethylamide
ALX-340-061-M005 5 mg

N-Arachidonoyl glycine
ALX-340-055-M005 5 mg

Arvanil BULK
ALX-340-042-M005 5 mg

„Hybrid" activator of CB_1 receptor (CB_1: K_i=0.5μM; CB_2: K_i=>15μM) and TRPV1 (K_i=0.3μM). Also inhibits anandamide uptake (IC_{50}=3.6μM) and fatty acid amide hydrolase (FAAH) (IC_{50}=3μM). Analgesic, vasodilatory and anti-inflammatory *in vivo.* Apoptosis inducer.

LIT: Unsaturated long-chain N-acyl-vanillyl-amides (N-AVAMs): vanilloid receptor ligands that inhibit anandamide-facilitated transport and bind to CB1 cannabinoid receptors: D. Melck, et al.; BBRC **262,** 275 (1999) ▪ Neurobehavioral activity in mice of N-vanillyl-arachidonyl-amide: V. Di Marzo, et al.; Eur. J. Pharmacol. **406,** 363 (2000)

Dihomo-γ-linolenylethanolamide
ALX-300-147-M005 5 mg

Docosatetraenylethanolamide
ALX-300-148-M005 5 mg

Linoleylethanolamide
ALX-300-149-M005 5 mg

Linvanil
ALX-340-044-M005 5 mg

Mead acid ethanolamide
ALX-300-151-M001 1 mg

R-1 Methanandamide
ALX-340-030-M005 5 mg

Amidase resistant cannabinoid receptor (CB) agonist (CB_1: K_i=20nM; CB_2: K_i=815nM). The most potent of the series of methyl-anandamides. About 4-fold higher binding affinity for cannabinoid receptor CB_1 than anandamide (Prod. No. ALX-340-029) in the presence of PMSF. Does also bind to TRPV1 (K_i=4.67μM).

LIT: (R)-methanandamide: a chiral novel anandamide possessing higher potency and metabolic stability: V. Abadji, et al.; J. Med. Chem. **37,** 1889 (1994) ▪ Head group analogs of arachidonylethanolamide, the endogenous cannabinoid ligand: A.D. Khanolkar, et al.; J. Med. Chem. **39,** 4515 (1996)

S-1 Methanandamide
ALX-340-031-M005 5 mg

CB_1 receptor agonist (K_i=175nM). About one-third as potent as anandamide (Prod. No. ALX-340-029).

LIT: (R)-methanandamide: a chiral novel anandamide possessing higher potency and metabolic stability: V. Abadji, et al.; J. Med. Chem. **37,** 1889 (1994)

R-2 Methanandamide
ALX-340-033-M005 5 mg

S-2 Methanandamide
ALX-340-034-M005 5 mg

Oleoylethanolamide [OEA] BULK
ALX-300-150-M005 5 mg

Activates TRPV1. Does not activate cannabinoid receptors (CB) but is a PPARα agonist (EC_{50}=120nM) *in vitro* and *in vivo;* induces satiety through activation of PPARα. Inhibits ceramidase.

LIT: Two new unsaturated fatty acid ethanolamides in brain that bind to the cannabinoid receptor: L. Hanus, et al.; J. Med. Chem. **36,** 3032 (1993) ▪ Differential regulation of sphingomyelinase and ceramidase activities by growth factors and cytokines. Implications for cellular proliferation and differentiation: E. Coroneos, et al.; J. Biol. Chem. **270,** 23305 (1995) ▪ Cannabinomimetic behavioral effects of and adenylate cyclase inhibition by two new endogenous anandamides: J. Barg, et al.; Eur. J. Pharmacol. **287,** 145 (1995) ▪ A peripheral mechanism for CB1 cannabinoid receptor-dependent modulation of feeding: R. Gomez, et al.; J. Neurosci. **22,** 9612 (2002) ▪ Activation of TRPV1 by the satiety factor oleoylethanolamide: G.P. Ahern; J. Biol. Chem. **278,** 30429 (2003) ▪ Oleylethanolamide regulates feeding and body weight through activation of the nuclear receptor PPAR-alpha: J. Fu, et al.; Nature **425,** 90 (2003) ▪ Oleoylethanolamide stimulates lipolysis by activating the nuclear receptor PPAR-alpha: M. Guzman, et al.; J. Biol. Chem. **279,** (2004)

See also "Latest Insight" on Page 4

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

„Hybrid" activator of CB_1 receptor (CB_1: K_i=1.6μM; CB_2: K_i=15μM) and TRVP1 (K_i=0.4μM; EC_{50}=33nM (human); EC_{50}=6.71nM (rat)). Also inhibits anandamide uptake (IC_{50}=9μM, K_i=14.1μM) and fatty acid amide hydrolase (FAAH) (IC_{50}=20μM).

LIT: NE-19550: a novel, orally active anti-inflammatory analgesic: L. Brand, et al.; Drugs Exp. Clin. Res. **13,** 259 (1987) ▪ The antinociceptive effect and pharmacokinetics of olvanil following oral and subcutaneous dosing in the mouse: W.K. Sietsema, et al.; Life Sci. **43,** 1385 (1988) ▪ Olvanil: more potent than capsaicin at stimulating the efferent function of sensory nerves: S.R. Hughes, et al.; Eur. J. Pharmacol. **219,** 481 (1992)

Palmitoylethanolamide BULK
ALX-300-146-M010 10 mg

Endogenous cannabinoid. Weak ligand of CB_1 (K_i=23.8μM) and CB_2 (K_i=13.9μM) receptor. Inhibits fatty acid amide hydrolase (FAAH) (IC_{50}=5.1μM). Immunosuppressant, anti-inflammatory, anti-nociceptive and anti-convulsant *in vivo.* The exact mode of action has not yet been revealed. It has been suggested that PEA: i) binds to a yet to be discovered cannabinoid receptor similar to CB_2; ii) administered *in vivo* elicits the synthesis of endogenous agonists of CB_2; iii) acts as an „entourage" compound by enhancing the activity and/or by influencing the turn-over of endogenous agonists of CB_2, possibly but not uniquely, by inhibiting their degradation.

LIT: Mast cells express a peripheral cannabinoid receptor with differential sensitivity to anandamide and palmitoylethanolamide: L. Facci, et al.; PNAS **92,** 3376 (1995)

Palmitoyl-N-isopropylamide
ALX-300-302-M005 5 mg

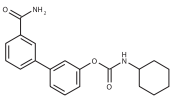
Inhibitor of fatty acid amide hydrolase (FAAH) (IC_{50}=12.8μM). Displays little binding to CB_1 and CB_2 receptors (IC_{50}>100μM) and very weakly blocks anandamide uptake (IC_{50}~100μM).

LIT: Effects of homologues and analogues of palmitoylethanolamide upon the inactivation of the endocannabinoid anandamide: K.O. Jonsson, et al.; Br. J. Pharmacol. **133,** 1263 (2001) ▪ AM404 and VDM 11 non-specifically inhibit C6 glioma cell proliferation at concentrations used to block the cellular accumulation of the endocannabinoid anandamide: K.O. Jonsson, et al.; Arch. Toxicol. **77,** 201 (2003)

FAAH & Related Products

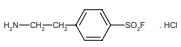
Fatty Acid Amide Hydrolase [FAAH] Inhibitors

URB597 BULK
ALX-550-382-M005 5 mg
ALX-550-382-M050 50 mg

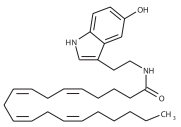

URB597

Potent inhibitor of fatty acid amide hydrolase (FAAH) (IC_{50}=4.6nM). Exhibits both anti-nociceptive and anxiolytic effects *in vivo* without evoking other symptoms associated with cannabinoid-like compounds.

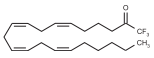
LIT: Molecular characterization of an enzyme that degrades neuromodulatory fatty-acid amides: B.F. Cravatt, et al.; Nature **384,** 83 (1996) ▪ Supersensitivity to anandamide and enhanced endogenous cannabinoid signaling in mice lacking fatty acid amide hydrolase: B.F. Cravatt, et al.; PNAS **98,** 9371 (2001) ▪ Modulation of anxiety through blockade of anandamide hydrolysis: S. Kathuria, et al.; Nat. Med. **9,** 76 (2003) ▪ Monoglyceride lipase-like enzymatic activity is responsible for hydrolysis of 2-arachidonoylglycerol in rat cerebellar membranes: S.M. Saario, et al.; Biochem. Pharmacol. **67,** 1381 (2004) ▪ Characterization of the fatty acid amide hydrolase inhibitor cyclohexyl carbamic acid 3'-carbamoyl-biphenyl-3-yl ester (URB597): effects on anandamide and oleoylethanolamide deactivation: D. Fegley, et al.; J. Pharmacol. Exp. Ther. **313,** 352 (2005) ▪ Actions of the FAAH inhibitor URB597 in neuropathic and inflammatory chronic pain models: A. Jayamanne, et al.; Br. J. Pharmacol. **147,** 281 (2006)


AEBSF . HCl

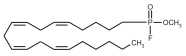
AEBSF . HCl BULK
ALX-270-022-M050 50 mg
ALX-270-022-M250 250 mg
ALX-270-022-G001 1 g


Arachidonoyl serotonin

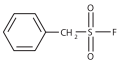
Arachidonoyl serotonin
ALX-340-060-M005 5 mg


Arachidonyl trifluoromethylketone

Arachidonoyl trifluoromethylketone
ALX-340-001-M005 5 mg
ALX-340-001-M010 10 mg
ALX-340-001-M050 50 mg


Methylarachidonyl fluorophosphonate

Methylarachidonyl fluorophosphonate
ALX-340-017-M001 1 mg
ALX-340-017-M005 5 mg


Phenylmethylsulfonyl fluoride

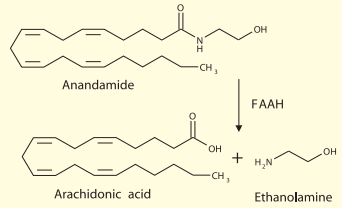
Phenylmethylsulfonyl fluoride BULK
ALX-270-184-G001 1 g
ALX-270-184-G005 5 g
ALX-270-184-G025 25 g

Related Products

PAb to Fatty Acid Amide Hydrolase
ALX-210-418-1 1 Vial

From rabbit. **IMMUNOGEN:** Synthetic peptide corresponding to aa 561-579 (C^{561}LR-FMREVEQLMTPQKQPS^{579}) of rat C-terminal FAAH (fatty acid amide hydrolase). **SPECIFICITY:** Recognizes human, mouse, rat and ferret FAAH. Detects a band of ~53kDa by Western blot. **APPLICATION:** IHC, WB. **BP:** ALX-156-005.

LIT: Fatty acid amide hydrolase is located preferentially in large neurons in the rat central nervous system as revealed by immunohistochemistry: K. Tsou, et al.; Neurosci. Lett. **254,** 137 (1998) ▪ Cannabinoids inhibit emesis through CB1 receptors in the brainstem of the ferret: M.D. Van Sickle, et al.; Gastroenterology **121**, 767 (2001)



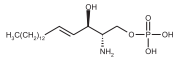
Fatty acid amide hydrolase (FAAH) is the enzyme responsible for hydrolysis and inactivation of fatty acid amides.

A Comprehensive Panel of Gangliosides & Sphingolipids

Sphingolipids were until not long ago thought to be little more than structural components of biological membranes and a potential reservoir for bioactive lipids. But recent studies have placed sphingolipids, including ceramide, sphingosine and sphingosine 1-phosphate, at the centre of a number of biological processeses, joining the well-established glycerolipid-derived mediators of signal transduction such as diacylglycerol, phosphatidylinositides and eicosanoids. Sphingolipid metabolism is clearly involved in the regulation of cell growth, differentiation, migration, angiogenesis, immunity and apoptosis. While ceramide and sphingosine usually inhibit proliferation and promote apoptosis, the further metabolite sphingosine 1-phosphate (1-SPP) stimulates growth and suppresses apoptosis. 1-SPP activates several widely expressed G protein coupled receptors (GPCR), but also plays a role as second messenger mobilizing Ca^{2+} independently of 1-SPP/GPCR binding.

Selected Review Articles

Sphingosine-1-phosphate: dual messenger functions: S.G. Payne, et al.; FEBS Lett. **531,** 54 (2002) ▪ Signalling and biological actions of sphingosine 1-phosphate: T. Hla; Pharmacol. Res. **47,** 401 (2003) ▪ Sphingolipids and the immune system: B. Cinque, et al.; Pharmacol. Res. **47,** 421 (2003) ▪ Sphingosine-1-phosphate: an enigmatic signalling lipid: S. Spiegel & S. Milstien; Nat. Rev. Mol. Cell Biol. **4,** 397(2003) ▪ Generation and metabolism of bioactive sphingosine-1-phosphate: H.L. Stunff, et al.; J. Cell. Biochem. **92,** 882 (2004) ▪ Biologically active sphingolipids in cancer pathogenesis and treatment: B. Ogretmen & Y.A. Hannun; Nat. Rev. Cancer **4,** 604 (2004) ▪ The complex life of simple sphingolipids: A.H. Futerman & Y.A. Hannun; EMBO Rep. **5,** 777(2004)

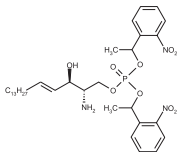


D-*erythro*-Sphingosine 1-phosphate (high purity) BULK

ALX-306-010-M001 1 mg
ALX-306-010-M005 5 mg

Purity: ≥99%. Synthetic. Sphingosine 1-phosphate (1-SPP) regulates a variety of cellular responses, including survival, cytoskeletal remodeling, chemotaxis etc. via the activation of cell surface EDG receptors. 1-SPP also promotes angiogenesis.

LIT: Sphingosine-1-phosphate in cell growth and cell death: S. Spiegel, et al.; Ann. NY Acad. Sci. 845, 11 (1998) ▪ For a comprehensive bibliography please visit our website.



D-*erythro*-Sphingosine 1-phosphate (caged)

ALX-306-017-C500 500 µg

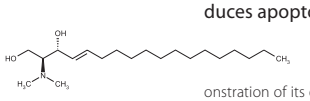
Synthetic. A photolyzable derivative of sphingosine 1-phosphate (1-SPP) (Prod. No. ALX-306-010). Important new tool for the study of 1-SPP mediated intracellular events.

LIT: Synthesis and evaluation of a photolyzable derivative of sphingosine 1- phosphate-caged SPP: L. Qiao, et al.; Bioorg. Med. Chem. Lett. 8, 711 (1998) ▪ Photolysis of intracellular caged sphingosine-1-phosphate causes Ca2+ mobilization independently of G-protein-coupled receptors.: D. Meyer zu Heringdorf, et al.; FEBS Lett. 554, 443 (2003) ▪ For a comprehensive bibliography please visit our website.

D-*erythro*-Sphingosine, N,N-Dimethyl-

ALX-306-009-M005 5 mg

Synthetic. Potent and specific inhibitor of sphingosine kinase (IC_{50}=5µM) which blocks conversion of sphingosine to sphingosine-1-phosphate (Prod. No. ALX-306-010). Inhibitor of protein kinase C (PKC) which also stimulates Src-kinase. May affect expression of cell surface selectins, which in turn mediate leukocyte or tumor cell adhesion to endothelial cells and platelets. Induces apoptosis.



LIT: A specific enhancing effect of N,N-dimethylsphingosine on epidermal growth factor receptor autophosphorylation. Demonstration of its endogenous occurrence (and the virtual absence of unsubstituted sphingosine) in human epidermoid carcinoma A431 cells: Y. Igarashi, et al.; J. Biol. Chem. **265,** 5385 (1990) ▪ For a comprehensive bibliography please visit our website.

Product Overview

Asialo-GM1
ALX-302-013-MC05 0.5 mg
ALX-302-013-M001 1 mg

Asialo-GM2
ALX-302-015-MC01 0.1 mg

Ceramide I (bovine brain)
ALX-303-001-M025 25 mg

Ceramide II (bovine brain)
ALX-303-002-M025 25 mg

Ganglioside GD1a . disodium salt (bovine brain)
ALX-302-007-M001 1 mg
ALX-302-007-M005 5 mg

Ganglioside GD1b . disodium salt (bovine brain)
ALX-302-009-M001 1 mg

Ganglioside GD3 . disodium salt (bovine brain)
ALX-302-010-MC05 0.5 mg
ALX-302-010-M001 1 mg

Ganglioside GM1 . sodium salt (bovine brain)
ALX-302-001-M001 1 mg
ALX-302-001-M005 5 mg
ALX-302-001-M010 10 mg

Ganglioside GM2 . sodium salt (bovine brain)
ALX-302-003-M001 1 mg

Ganglioside GM3 . sodium salt (bovine brain)
ALX-302-005-M001 1 mg

Ganglioside GM3 (Neu5Gc) (mouse hybridoma cells)
ALX-302-019-MC01 0.1 mg

Ganglioside GM3 (Neu5Ac) (CHO cells)
ALX-302-018-MC05 0.5 mg

Ganglioside GQ1b . tetrasodium salt (bovine brain)
ALX-302-012-MC01 0.1 mg
ALX-302-012-MC05 0.5 mg

Ganglioside GT1b . trisodium salt (bovine brain)
ALX-302-011-M001 1 mg
ALX-302-011-M005 5 mg

Gangliosides (mixture) (mouse brain)
ALX-302-017-M001 1 mg

GM1 Pentasaccharide . sodium salt
ALX-305-006-M001 1 mg

MSDH-C
ALX-303-005-M001 1 mg

Neutral Glycosphingolipids (human granulocytes)
ALX-306-026-M001 1 mg

Psychosine
ALX-306-004-M005 5 mg

D-*erythro*-Sphingomyelin (bovine brain)
ALX-306-001-M250 250 mg
ALX-306-001-G001 1 g

D-*erythro*-Sphingosine (isolated)
ALX-306-002-M050 50 mg

D-*erythro*-Sphingosine (synthetic)
ALX-306-011-M005 5 mg
ALX-306-011-M025 25 mg

D-*erythro*-Sphingosine, N-Acetyl-
ALX-306-024-M005 5 mg

D-*erythro*-Sphingosine, N-Hexanoyl-
ALX-303-003-M001 1 mg
ALX-303-003-M005 5 mg

D-*erythro*-Sphingosine, N-Octanoyl-
ALX-306-013-M005 5 mg

D-*erythro*-Sphingosine, N-Palmitoyl- (synthetic)
ALX-306-025-M001 1 mg
ALX-306-025-M005 5 mg

Sphingosine 1-phosphate, (2S,3R)-Dihydro-
ALX-306-016-C500 500 µg
ALX-306-016-M001 1 mg

For other Sphingosine Derivatives please visit www.axxora.com

Antibodies

MAb to Ceramide (MID 15B4)

ALX-804-196-T050 50 tests

CLONE: MID 15B4. **ISOTYPE:** Mouse IgM. **IMMUNOGEN:** Ceramide (sphingosine-[*trans*-D-*erythro*-2-amino-4-octadecene-1,3-diol]) conjugated to BSA. **SPECIFICITY:** Recognizes C16- and C24-ceramide, dihydroceramide, sphingomyelin and phosphatidylcholine in highly artificial lipid overlay test systems. Under more physiological *in vitro* and *in vivo* conditions highly specific for ceramide and does not cross-react with sphingomyelin, cholesterol or other phospholipids. **APPLICATION:** ELISA, FC, IHC.

LIT: Structural determinants of sphingolipid recognition by commercially available anti-ceramide antibodies: L.A. Cowart, et al.; J. Lipid Res. **43,** 2042 (2002) ▪ CD95 Signaling Via Ceramide-rich Membrane Rafts: H. Grassme, et al.; J. Biol. Chem. **276,** 20589 (2002) ▪ Ceramide-Rich Membrane Rafts Mediate CD40 Clustering: H. Grassme, et al.; J. Immunol. **168,** 298 (2002)

MAb to Ganglioside GD2 (11H3)

CVL-MAB0030-1 1 Vial

CLONE: 11H3. **ISOTYPE:** Mouse IgG3. **IMMUNOGEN:** Ganglioside GD2. **SPECIFICITY:** Recognizes ganglioside GD2. **APPLICATION:** ELISA, WB.

MAb to Ganglioside GD3 (4F6)

CVL-MAB0014-1 1 Vial

CLONE: 4F6. **ISOTYPE:** Mouse IgG3. **IMMUNOGEN:** Ganglioside GD3. **SPECIFICITY:** Recognizes ganglioside GD3. Cross-reacts with 9-O-AcGD3 and ganglioside GT1a. **APPLICATION:** ELISA, WB.

MAb to Ganglioside OAcGD3 (7H2)

CVL-MAB0015-1 1 Vial

CLONE: 7H2. **ISOTYPE:** Mouse IgG3. **IMMUNOGEN:** Ganglioside OAcGD3. **SPECIFICITY:** Recognizes ganglioside OAcGD3. **APPLICATION:** ELISA, WB.

PRODUCT SPECIFIC LIT: Shedding of GD2 ganglioside in patients with retinoblastoma: J. Portoukalian, et al.; Int. J. Cancer **53,** 948 (1993) ▪ Deficiency of ganglioside biosynthesis in metastatic human melanoma cells: relevance of CMP-NeuAc: LacCer alpha 2-3 sialyltransferase (GM3 synthase): N. Zebda, et al.; FEBS Lett. **362,** 161 (1995) ▪ Gangliosides protect human melanoma cells from ionizing radiation-induced clonogenic cell death: C.P. Thomas, et al.; Glycoconj. J. **13,** 377 (1996) ▪ Variable region gene segments of nine monoclonal antibodies specific to disialogangliosides (GD2, GD3) and their O-acetylated derivatives: E. Cerato, et al.; Hybridoma **16,** 307 (1997)

Potent γ-Secretase Inhibitors

Selected Review Articles

γ-Secretase inhibitors as molecular probes of presenilin function: M.S. Wolfe; J. Mol. Neurosci. **17,** 199 (2001)

γ-secretase inhibition: D. Beher & M.S. Shearman; Biochem. Soc. Trans. **30,** 534 (2002)

γ-secretase inhibitors and Alzheimer's disease: S.B. Roberts; Adv. Drug Deliv. Rev. **54,** 1579 (2002)

The search for γ-secretase and development of inhibitors: J.Y. Tsai, et al.; Curr. Med. Chem. **9,** 1087 (2002)

γ-secretase inhibitors – from molecular probes to new therapeutics?: T. Harrison & D. Beher; Prog. Med. Chem. **41,** 99 (2003)

γ-secretase as a target for drug intervention in Alzheimer's disease: T. Harrison et al.; Curr. Opin. Drug Discov. Devel. **7,** 709 (2004)

γ-secretase as a therapeutic target for the treatment of Alzheimer's disease: I. Churcher & D. Beher; Curr. Pharm. Des. **11,** 3363 (2005)

Concepts for the treatment of Alzheimer's disease: molecular mechanisms and clinical application: C. Pietrzik & C. Behl; Int. J. Exp. Pathol. **86,** 173 (2005)

Compound E — BULK

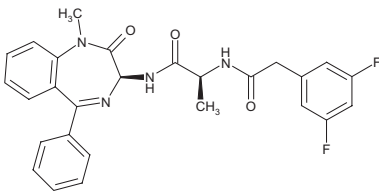
[(2S)-2-{[(3,5-Difluorophenyl)acetyl]amino}-*N*-[(3S)-1-methyl-2-oxo-5-phenyl-2,3-dihydro-1*H*-1,4-benzodiazepin-3-yl]propanamide]

ALX-270-415-C250 250 µg
ALX-270-415-M001 1 mg

NEW

Now available from stock – reduced prices! Step up to the Source™

- Compound E was first described by Seiffert et al. 2000 and applies today as a standard γ-secretase inhibitor.
- Cell permeable.
- Potent, selective, non-transition state and non-competitive inhibitor of γ-secretase and Notch processing.
- IC_{50} = 0.3 nM for total β-amyloid.
- At higher concentrations (200-400 µM) only weakly affects the presenilinase activity.
- Activity tested!



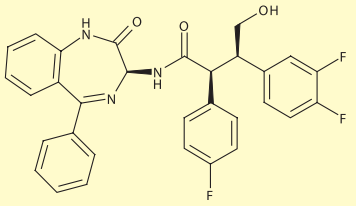
Compound 34 — BULK

[(2*S*,3*R*)-3-3,4-Difluorophenyl)-2-(4-fluorophenyl)-4-hydroxy-*N*-((3S)-2-oxo-5-phenyl-2,3-1*H*-benzo[e][1,4]diazepin-3-yl)butyramide]

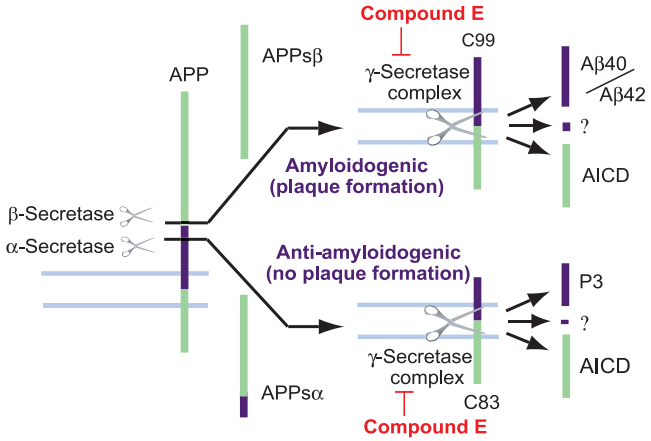
ALX-270-417-C200 200 µg
ALX-270-417-M001 1 mg

Cell permeable, highly potent inhibitor of γ-secretase (IC_{50}=0.06nM).

LIT: Design and synthesis of highly potent benzodiazepine gamma-secretase inhibitors: preparation of (2S,3R)-3-(3,4-difluorophenyl)-2-(4-fluorophenyl)-4- hydroxy-N-((3S)-1-methyl-2-oxo-5- phenyl-2,3-dihydro-1H-benzo[e][1,4]-diazepin-3-yl)but: I. Churcher, et al.; J. Med. Chem. **46,** 2275 (2003)



LIT: Presenilin-1 and -2 are molecular targets for γ-secretase inhibitors: D. Seiffert, et al.; J. Biol. Chem. **275,** 34086 (2000) ▪ Pharmacological knock-down of the presenilin 1 heterodimer by a novel γ-secretase inhibitor: implications for presenilin biology: D. Beher, et al.; J. Biol. Chem. **276,** 45394 (2001) ▪ Presenilin-dependent γ-secretase activity modulates thymocyte development: P. Doerfler, et al.; PNAS **98,** 9312 (2001) ▪ γ-Secretase cleavage and nuclear localization of ErbB-4 receptor tyrosine kinase: C.Y. Ni, et al.; Science **294,** 2179 (2001) ▪ aph-1 and pen-2 are required for Notch pathway signaling, γ-secretase cleavage of betaAPP, and presenilin protein accumulation: R. Francis, et al.; Dev. Cell **3,** 85 (2002) ▪ Presenilin-dependent γ-secretase-like intramembrane cleavage of ErbB4: H.J. Lee, et al.; J. Biol. Chem. **277,** 6318 (2002) ▪ Linear non-competitive inhibition of solubilized human γ-secretase by pepstatin A methylester, L685458, sulfonamides, and benzodiazepines: G. Tian, et al.; J. Biol. Chem. **277,** 31499 (2002) ▪ Regulated intramembrane proteolysis of the p75 neurotrophin receptor modulates its association with the TrkA receptor: K.M. Jung, et al.; J. Biol. Chem. **278,** 42161 (2003) ▪ Presenilin-dependent γ-secretase activity mediates the intramembranous cleavage of CD44: D. Murakami, et al.; Oncogene **22,** 1511 (2003) ▪ Nicastrin, presenilin, APH-1, and PEN-2 form active γ-secretase complexes in mitochondria: C.A. Hansson, et al.; J. Biol. Chem. **279,** 51654 (2004) ▪ Activating mutations of NOTCH1 in human T cell acute lymphoblastic leukemia: A.P. Weng, et al.; Science **306,** 269 (2004) ▪ Identification of a new presenilin-dependent zeta-cleavage site within the transmembrane domain of amyloid precursor protein: G. Zhao, et al.; J. Biol. Chem. **279,** 50647 (2004) ▪ Linking receptor-mediated endocytosis and cell signaling: evidence for regulated intramembrane proteolysis of megalin in proximal tubule: Z. Zou, et al.; J. Biol. Chem. **279,** 34302 (2004) ▪ Determination of guinea-pig cortical γ-secretase activity ex vivo following the systemic administration of a gamma-secretase inhibitor: S. Grimwood, et al.; Neuropharmacology **48,** 1002 (2005)



Parkinson's Disease

NEW PAb to LRRK2 (human) (AT106)

ALX -210-928-C100 100 µg

From rabbit. **IMMUNOGEN:** Human LRRK2 (leucine-rich repeat kinase 2) (aa 1838-2133) is fused at the N-terminus to a tag. **SPECIFICITY:** Recognizes human LRRK2. **APPLICATION:** IP, WB.

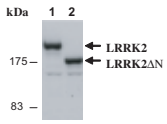


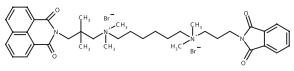
FIGURE: Detection of human LRRK2 by PAb to LRRK2 (human) (AT106) (Prod. No. ALX-210-928).

Allosteric M2 Muscarinic Acetylcholine Receptor Ligands

NEW Naphmethonium dibromide

ALX-550-401-M005 5 mg

Potent allosteric modulator of M2 muscarinic acetylcholine receptor. Retards the dissociation of the antagonist n-methylscopolamine and exhibits positive cooperativity, i.e. shows higher affinity for occupied receptors compared to free receptors. Affinity for the free receptor is about 100-fold higher than with W84.

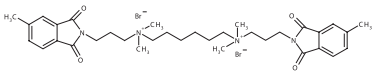


LIT: Systematic development of high affinity bis(ammo-nio)alkane-type allosteric enhancers of muscarinic ligand binding: M. Muth, et al.; J. Med. Chem. **46,** 1031 (2003)

NEW Dimethyl-W84 dibromide

ALX-550-400-M005 5 mg

Potent allosteric modulator of M2 muscarinic acetylcholine receptor. Retards the dissociation of the antagonist n-methylscopolamine. Affinity for the free receptor is about 10-fold higher than with W84.

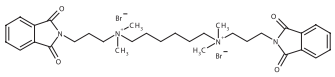


LIT: Identification of a [3H]Ligand for the common allosteric site of muscarinic acetylcholine M2 receptors: C. Trankle, et al.; Mol. Pharmacol. **54,** 139 (1998) ▪ Interactions of orthosteric and allosteric ligands with [3H]dimethyl-W84 at the common allosteric site of muscarinic M2 receptors: C. Trankle, et al.; Mol. Pharmacol. **64,** 180 (2003) ▪ Allosteric site on muscarinic acetylcholine receptors: identification of two amino acids in the muscarinic M2 receptor that account entirely for the M2/M5 subtype selectivities of some structurally diverse allosteric ligands in N-methylscopolamine-occupie: U. Voigtlander, et al.; Mol. Pharmacol. **64,** 21 (2003)

NEW W84 dibromide

ALX-550-399-M005 5 mg

Potent allosteric modulator of M2 muscarinic acetylcholine receptor. Retards the dissociation of the antagonist n-methylscopolamine.



LIT: Search for lead structures to develop new allosteric modulators of muscarinic receptors: C. Trankle, et al.; J. Pharmacol. Exp. Ther. **279,** 926 (1996) ▪ Muscarinic allosteric enhancers of ligand binding: pivotal pharmacophoric elements in hexamethonio-type agents: M. Muth, et al.; J. Med. Chem. **48,** 2212 (2005)

Dopamine-β-hydroxylase [DBH]

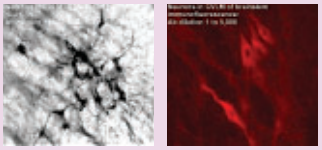
The copper enzyme dopamine β-hydroxylase (DBH; dopamine β-mono-oxygenase, EC 1.14.17.1) is a mixed-function oxidase catalysing the last step in the biosynthesis of noradrenaline.

LIT: Congenital dopamine-beta-hydroxylase deficiency in humans: H.J. Timmers, et al.; Ann. N. Y. Acad. Sci. **1018,** 520 (2004) ▪ Human genetics of plasma dopamine beta-hydroxylase activity: applications to research in psychiatry and neurology: J.F. Cubells and C.P. Zabetian; Psychopharmacology (Berlin) **174,** 463 (2004)

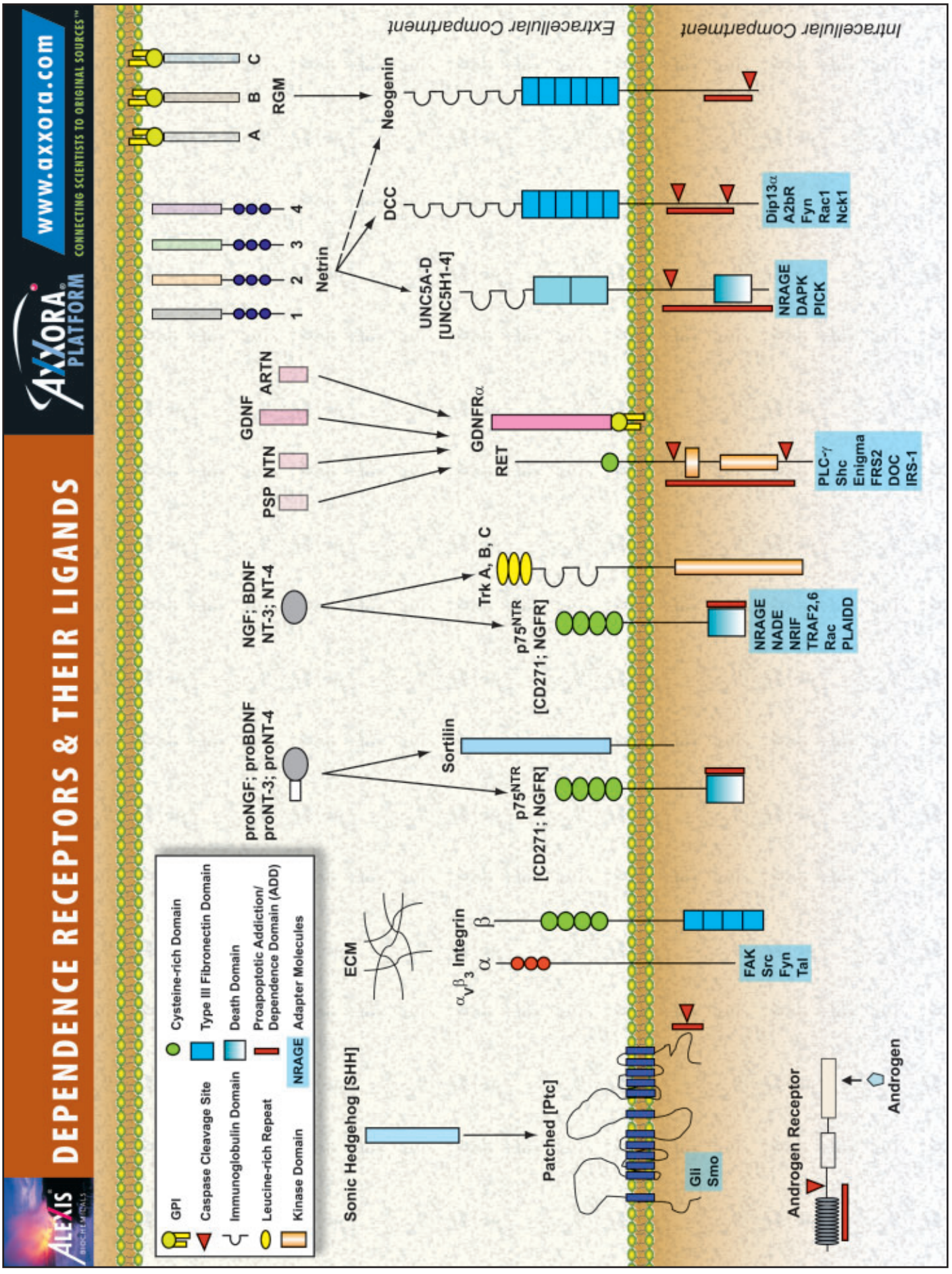
NEW PAb to Dopamine-β-hydroxylase [DBH]

ALX-210-560-R250 250 µl

From rabbit. **IMMUNOGEN:** Synthetic peptide corresponding to N-terminal aa 43-62 (S^{43}EPPESPFPYHIPLDPEGTL^{62}) of rat dopamine-β-hydroxylase (DBH). This sequence is highly conserved (>85% homology) in human, bovine and mouse DBH. **SPECIFICITY:** Recognizes rat DBH (broad species cross-reactivity is expected due to conservation of the immunogenetic sequence). Specifically stains chromaffin cells of the adrenal medulla and DBH-containing cells of the sympathetic nervous system, including locus coeruleus and medulla oblangata. **APPLICATION:** ICC, IHC (FS), WB.



Purified (PF) = Purified (Preservative free); FC = Flow Cytometry; ICC = Immunocytochemistry; IP = Immunoprecipitation; IHC = Immunohistochemistry (FS = Frozen Sections, PS = Paraffin Sections); WB = Western blot; BP = Blocking Peptide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Extracellular Compartment
GPI
Caspase Cleavage Site
Cysteine-rich Domain
Type III Fibronectin Domain
Immunoglobulin Domain
Death Domain
Leucine-rich Repeat
Proapoptotic Addiction/ Dependence Domain (ADD)
Kinase Domain
NRAGE
Adapter Molecules
Sonic Hedgehog [SHH]
Patched [Ptc]
Gli
Smo
ECM
$\alpha_v\beta_3$ Integrin
α
β
FAK
Src
Fyn
Tal
proNGF; proBDNF
proNT-3; proNT-4
Sortilin
p75NTR
[CD271; NGFR]
NGF; BDNF
NT-3; NT-4
Trk A, B, C
p75NTR
[CD271; NGFR]
NRAGE
NADE
NRIF
TRAF2,6
Rac
PLAIDD
PSP
NTN
GDNF
ARTN
GDNFRα
RET
PLC-γ
Shc
Enigma
FRS2
DOC
IRS-1
Netrin
UNC5A-D
[UNC5H1-4]
DCC
Neogenin
1
2
3
4
A
B
C
RGM
NRAGE
DAPK
PICK
Dip13α
A2bR
Fyn
Rac1
Nck1
Androgen Receptor
Androgen

Related Products

Nerve Growth Factor Receptor [NGFR; p75^{NTR}; TNFRSF16]

NGFR/p75^{NTR} (human):Fc (human) (rec.)
ALX-522-044-C050 50 µg
Produced in HEK 293 cells. The extracellular cysteine-rich domain of human NGFR (nerve growth factor receptor; p75^{NTR}) (aa 1-264) is fused to the Fc portion of human IgG1.

NEW MAb to NGFR/p75^{NTR} (human) (Nagy-1)
ALX-804-833-C100 100 µg
CLONE: Nagy-1. **ISOTYPE:** Rat IgG2a. **IMMUNOGEN:** Recombinant human NGFR (nerve growth factor receptor; p75^{NTR}):Fc (Prod. No. ALX-522-044). **SPECIFICITY:** Recognizes human NGFR. **APPLICATION:** FC, IP.

NEW MAb to NGFR/p75^{NTR} (human) (MGR15)
ALX-804-574-C050 50 µg
CLONE: MGR15. **ISOTYPE:** Mouse IgM. **IMMUNOGEN:** SKNBE neuroblastoma cell line transfected with human NGFR (nerve growth factor receptor; p75^{NTR}). **SPECIFICITY:** Recognizes an epitope present in the extracellular domain of human NGFR. **APPLICATION:** FC, IHC (FS).

NEW PAb to NGFR/p75^{NTR} (human) (AT101)
ALX -210-921-C050 50 µg
From rabbit. **IMMUNOGEN:** Recombinant human NGFR (nerve growth factor receptor; p75^{NTR}):Fc (Prod. No. ALX-522-044). **SPECIFICITY:** Recognizes human NGFR. **APPLICATION:** WB. Note: Does not work for IP.

NGF

pro-β-Nerve Growth Factor (human) (rec.)
ALX-201-207-C020 20 µg
Produced in *E. coli*. **BIOLOGICAL ACTIVITY:** Stimulates the proliferation of TF1 cells (EC_{50}=130±30pM).

β-Nerve Growth Factor (human) (rec.)
ALX-201-208-C020 20 µg
Produced in *E. coli*. **BIOLOGICAL ACTIVITY:** Stimulates the proliferation of TF1 cells (EC_{50}=10.9±2.7pM).

TrkA

NEW MAb to TrkA (human) (MGR12)
ALX-804-575-C100 100 µg
CLONE: MGR12. **ISOTYPE:** Mouse IgG1. **IMMUNOGEN:** SKNBE neuroblastoma cell line transfected with human TrkA. **SPECIFICITY:** Recognizes an epitope present in the extracellular domain of human TrkA. Detects a band of ~140kDa by IP. **APPLICATION:** FC, IHC (FS), IP.

LIT: Production of a monoclonal antibody directed against the high-affinity nerve growth factor receptor: E. Tagliabue, et al.; Int. J. Biol. Markers **14,** 68 (1999)

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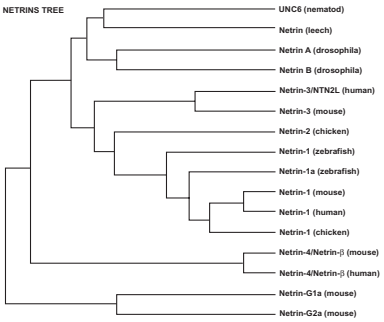
Netrin-1 & Its Receptors

The netrins (whose name means "one who guides" in Sanskrit) are a family of laminin-related secreted proteins. The following netrins have so far been described:



In neuronal development netrin-1 is predominantly expressed by floor plate cells as commissural axons extend toward the ventral midline. Netrin-1 induces axonal outgrowth, axon orientation and neuronal migration. It is chemoattractive for some neurons and chemorepellent for others.

Netrin-1 is also expressed in organs such as pancreas, lung, bowel, bone and mammary gland. In these tissues, netrin-1 has different roles such as invasion of epithelial cells, leukocytes migration, cell adhesion or angiogenesis. As a survival factor, netrin-1 contributes to the control of tumorigenesis.

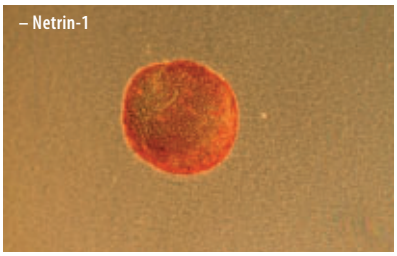
To carry its functions, netrin-1 interacts with specific receptors that belong to two protein families: DCC / neogenin and UNC5H. These receptors belong to the family of "dependence receptors" that induce apoptosis in the absence of their respective ligand, and promote survival when bound to their ligand. The netrin-1 mediated survival signal inhibits p53-induced apoptosis.

Selected Review Articles

Netrin-1 and its receptors in tumorigenesis: Arakawa, H.; Nat. Rev. Cancer **4,** 978 (2004)

Netrin-1: when a neuronal guidance cue turns out to be a regulator of tumorigenesis: P. Mehlen and C. Furne; Cell. Mol. Life Sci. **62,** 2599 (2005)

The Netrin family of guidance factors: emphasis on Netrin-1 signalling: M.J. Barallobre, et al.; Brain Res. Rev. **49,** 22 (2005)



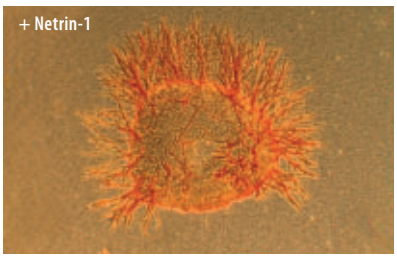


FIGURE: Netrin-1 (human) (rec.) (Prod. No. ALX-522-100) mediated commissural axon outgrowth.

METHOD: Dorsal spinal cord was dissected out from E13 rat embryos and cultured in collagen matrix in the presence or absence of Netrin-1 (250 ng/ml). Axons were then stained with an anti-β-tubulin antibody.

Picture courtesy of Véronique Corset, Centre Léon Bérard, Lyon.

Product Highlight!

NEW Netrin-1 (human) (rec.)
ALX-522-100-2010 2 x 10 µg
Produced in HEK 293 cells. Human netrin-1 (aa 28-604) is fused at the N-terminus to a FLAG®-tag. **SPECIFICITY:** Binds to human, mouse and rat receptors UNC5H and DCC. **BIOLOGICAL ACTIVITY:** Induces axon outgrowth. Inhibits DCC- and UNHC5H2-mediated apoptosis in HEK293 cells.

Ask for Bulk Quantities!

Netrin Receptor

NEW UNC5B (human): Fc (human) (rec.)
[UNC5H2 (human): Fc (human) (rec.)]
ALX-522-095-C050 50 µg
Produced in CHO cells. The extracellular domain of UNC5B (UNC5H2) (aa 28-363) is fused to the Fc portion of human IgG1. **SPECIFICITY:** Binds to human, mouse and chicken netrin-1 and to chicken netrin-2. Inhibits netrin-1 mediated survival of HEK 293 cells overexpressing DCC or UNC5B.

Antibody

NEW MAb to Netrin-1 (human) (Nora-1)
ALX-804-838-C100 100 µg
CLONE: Nora-1. **ISOTYPE:** Mouse IgG2a. **IMMUNOGEN:** Recombinant human netrin-1 (aa 28-604) fused at the N-terminus to a tag. **SPECIFICITY:** Recognizes human netrin-1. **APPLICATION:** ELISA, WB.

Repulsive Guidance Molecules [RGMs]

RGMs are involved in neuronal development and bone morphogenetic protein (BMP) signalling.

LIT: Iron metabolism meets signal tranduction: G.J. Anderson & D.M. Frazer; Nat. Genetics **38,** 503 (2006)

RGMA, Soluble (human) (rec.)
[Repulsive Guidance Molecule A, Soluble]
ALX-522-103-2010 2 x 10 µg
Produced in HEK 293 cells. The domain of human RGMA (aa 48-422) is fused at the N-terminus to a linker peptide (8aa) and a FLAG-tag.

RGMC (human) (rec.)
[Repulsive Guidance Molecule C, Soluble; Hemojuvelin]
ALX-522-104-C010 10 µg
Produced in HEK 293 cells. The domain of human RGMC (aa 36-398) is fused at the N-terminus to a linker peptide (8aa) and a FLAG-tag.

Metabotropic Glutamate Receptors [mGLRs]

L-Glutamate is the major excitatory neurotransmitter in mammalian central nervous systems, acting on complex signalling cascades through ligand gated channels (ionotropic receptors) and G protein coupled (metabotropic) receptors (mGluRs).

The mGluRs have been classified into three groups, based on sequence similarity, pharmacology and intercellular signalling. Group I mGluRs (mGluR1 and mGluR5) couple to Gq proteins to activate phospholipase C (PLC) and triggering the release of Ca^{2+} from intracellular stores (e.g. ER), while decreasing the intracellular K^+ concentration. Group II mGluRs (mGluR2 and mGluR3) couple to Gi proteins to negatively regulate the activity of adenylyl cyclase. Group III mGluRs (mGluR4, mGluR6, mGluR7, and mGluR8) act as autoreceptors and are also coupled to Gi proteins to decrease adenylyl cyclase activity or increasing the intracellular Ca^{2+} concentration.

Extensive research into the functions of mGluRs has shown their essential role in normal brain functions, but also in neurological and psychiatric disorders. The precise functions of these receptors remain uncertain. The development of selective ligands with appropriate pharmacokinetic properties is essential for a better understanding of the mGluRs and the signalling cascades.

Selected Review Articles

Identification and functional roles of metabotropic glutamate receptor-interacting proteins: L. Fagni, et al.; Semin. Cell Dev. Biol. **15,** 289 (2004) ▪ The ups and downs of addiction: role of metabotropic glutamate receptors: P.J. Kenny & A. Markou; TIPS **25,** 265 (2004) ▪ Positive and negative allosteric modulation of metabotropic glutamate receptors: emerging therapeutic potential: J.N. Kew; Pharmacol. Ther. **104,** 233 (2004) ▪ Metabotropic glutamate receptors in the basal ganglia motor circuit: P.J. Conn, et al.; Nat. Rev. Neurosci. **6,** 787 (2005) ▪ New therapeutic frontiers for metabotropic glutamate receptors: C.M. Niswender, et al.; Curr. Top. Med. Chem. **5,** 847 (2005) ▪ Positive allosteric modulators of the metabotropic glutamate receptor subtype 2 (mGluR2): M.T. Rudd & J.A. McCauley; Curr. Top. Med. Chem. **5,** 869 (2005) ▪ Recent advances in non-competitive mGlu5 receptor antagonists and their potential therapeutic applications: A. Slassi, et al.; Curr. Top. Med. Chem. **5,** 897 (2005) ▪ Metabotropic glutamate receptors as novel targets for anxiety and stress disorders: C.J. Swanson, et al.; Nat. Rev. Drug Discov. **4,** 131 (2005) ▪ The role of group I metabotropic glutamate receptors in neuronal excitotoxicity in Alzheimer's disease: V.W. Tsai, et al.; Neurotox. Res. **7,** 125 (2005) ▪ Discovery of positive allosteric modulators of metabotropic glutamate receptor subtype 5 (mGluR5): D.L. Williams, Jr. & C.W. Lindsley; Curr. Top Med. Chem. **5,** 825 (2005) ▪ Agonists and antagonists for group III metabotropic glutamate receptors 6, 7 and 8: Z.Q. Yang; Curr. Top Med. Chem. **5,** 913 (2005)

Potent and Selective mGluR5 Antagonists

MTEP — BULK

[3-[(2-Methyl-1,3-thiazol-4-yl)ethynyl]pyridine]

ALX-550-381-M005	5 mg
ALX-550-381-M025	25 mg

Potent and selective antagonist for mGluR5 with a 5-fold higher anxiolytic activity than MPEP (Prod. No. ALX-550-368). Shows fewer off-target effects than MPEP.

LIT: [3H]Methoxymethyl-3-[(2-methyl-1,3-thiazol-4-yl)ethynyl]-pyridine binding to metabotropic glutamate receptor subtype 5 in rodent brain: in vitro and in vivo characterization: J.J. Anderson, et al.; J. Pharmacol. Exp. Ther. **303,** 1044 (2002) ▪ Reduced stress-induced hyperthermia in mGluR5 knockout mice: J. Brodkin, et al.; Eur. J. Neurosci. **16,** 2241 (2002) ▪ Neuroprotective activity of the mGluR5 antagonists MPEP and MTEP against acute excitotoxicity differs and does not reflect actions at mGluR5 receptors: P.M.t. Lea, et al.; Br. J. Pharmacol. **145,** 527 (2005) ▪ MTEP, a new selective antagonist of the metabotropic glutamate receptor subtype 5 (mGluR5), produces antiparkinsonian-like effects in rats: K. Ossowska, et al.; Neuropharmacology **49,** 447 (2005) ▪ Potential antidepressant-like effect of MTEP, a potent and highly selective mGluR5 antagonist: A. Palucha, et al.; Pharmacol. Biochem. Behav. **81,** 901 (2005) ▪ In vitro metabolic studies on the selective metabotropic glutamate receptor sub-type 5 (mGluR5) antagonist 3-[(2-methyl-1,3-thiazol-4-yl) ethynyl]-pyridine (MTEP): M.D. Green, et al.; Neurosci. Lett. **391,** 91 (2006) ▪ **For a comprehensive bibliography please visit our website.**

MPEP . HCl — BULK

[6-Methyl-2-(phenylethynyl)-pyridine . HCl]

ALX-550-368-M005	5 mg
ALX-550-368-M025	25 mg

Potent and selective antagonist for mGluR5. Systemically active *in vivo*.

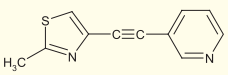
LIT: 2-Methyl-6-(Phenylethynyl)-pyridine (MPEP), a potent, selective and systemically active MGlu5 receptor antagonist: F. Gasparini, et al.; Neuropharmacology **38,** 1493 (1999) ▪ Antagonism of the mGlu5 agonist 2-chloro-5-hydroxyphenylglycine by the novel selective mGlu5 antagonist 6-methyl-2-(phenylethynyl)-pyridine (MPEP) in the thalamus: T.E. Salt, et al.; Br. J. Pharmacol. **127,** 1057 (1999) ▪ Pharmacological agents acting at subtypes of metabotropic glutamate receptors: D.D. Schoepp, et al.; Neuropharmacology **38,** 1431 (1999) ▪ Selective blockade of metabotropic glutamate receptor subtype 5 is neuroprotective: V. Bruno, et al.; Neuropharmacology **39,** 2223 (2000) ▪ Anticonvulsant activity of two metabotropic glutamate group I antagonists selective for the mGlu5 receptor: 2-methyl-6-(phenylethynyl)-pyridine (MPEP), and (E)-6-methyl-2-styryl-pyridine (SIB 1893): A.G. Chapman, et al.; Neuropharmacology **39,** 1567 (2000) ▪ Methylphenylethynylpyridine (MPEP) Novartis: F. Micheli; Curr. Opin. Investig. Drugs **1,** 355 (2000) ▪ **For a comprehensive bibliography please visit our website.**

NEW Fenobam

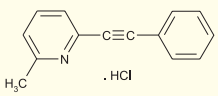
ALX-550-413-M005	5 mg
ALX-550-413-M025	25 mg

Potent and selective non-competitive mGluR5 antagonist that displays inverse agonist properties; blocks mGluR5 constitutive activity *in vitro* (IC_{50}=87nM). Acts at an allosteric modulatory site shared with MPEP (Prod. No. ALX-550-368) and binds mGluR5 with Kd values of 54nM and 31nM for rat and human receptors respectively. Displays anxiolytic activity following oral administration *in vivo*.

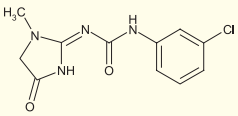
LIT: Novel non-benzodiazepine anxiolytics: M. E. Goldberg, et al.; Neuropharmacology **22,** 1499 (1983) ▪ In vitro and in vivo metabolism of the antianxiolytic agent fenobam in the rat: W. N. Wu, et al.; J. Pharm. Sci. **84,** 185 (1995) ▪ Fenobam: a clinically validated nonbenzodiazepine anxiolytic is a potent, selective, and noncompetitive mGlu5 receptor antagonist with inverse agonist activity: R. H. Porter, et al.; J. Pharmacol. Exp. Ther. **315,** 711 (2005) ▪ Phenyl ureas of creatinine as mGluR5 antagonists. A structure-activity relationship study of fenobam analogues: A. Wallberg, et al.; Bioorg. Med. Chem. Lett. **16,** 1142 (2006)



MTEP



MPEP . HCl



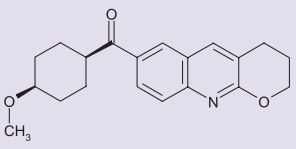
Fenobam

Potent Non-competitive mGluR1 Antagonists

NEW JNJ 16259685

ALX-550-412-M005	5 mg
ALX-550-412-M025	25 mg

Sub-nanomolar potent, non-competitive mGluR1 antagonist (K_i=0.34nM). Inhibits glutamate-induced Ca^{2+} response at the human mGluR1 with an IC_{50} value of 0.55nM. Selective over mGluR5 (> 400-fold) and displays no activity at mGluR2, mGluR3, mGluR4, mGluR6, AMPA or NMDA receptors (IC_{50} > 10µM). Centrally active following systemic administration.



LIT: JNJ16259685, a highly potent, selective and systemically active mGlu1 receptor antagonist: H. Lavreysen, et al.; Neuropharmacology **47,** 961 (2004) ▪ Effects of mGlu1 receptor blockade on anxiety-related behaviour in the rat lick suppression test: T. Steckler, et al.; Psychopharmacology (Berl.) **179,** 198 (2005) ▪ Metabotropic glutamate receptor 1 blockade impairs acquisition and retention in a spatial Water maze task: T. Steckler, et al.; Behav. Brain Res. **164,** 52 (2005) ▪ Synthesis, structure-activity relationship, and receptor pharmacology of a new series of quinoline derivatives acting as selective, noncompetitive mGlu1 antagonists: D. Mabire, et al.; J. Med. Chem. **48,** 2134 (2005)

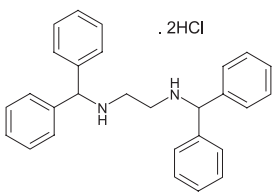
First Selective mGluR7 Agonist

NEW AMN082 . 2HCl

ALX-550-414-M005	5 mg
ALX-550-414-M025	25 mg

The first selective mGluR7 agonist. Potently inhibits cAMP accumulation and stimulates GTP-γ-S binding in recombinant cells and on membranes expressing mGluR7 (EC_{50}=64-290nM). Selective over other mGluR subtypes and selected ionotropic glutamate receptors up to 10µM. Acts via a novel allosteric site and is orally active and brain penetrant.

LIT: A selective metabotropic glutamate receptor 7 agonist: activation of receptor signaling via an allosteric site modulates stress parameters in vivo: K. Mitsukawa, et al.; PNAS **102,** 18712 (2005)



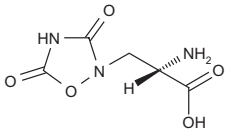
Potent Group I mGluR Agonist

L-Quisqualic acid — BULK

ALX-550-059-M005	5 mg
ALX-550-059-M025	25 mg

Potent group I mGluR agonist and quisqualate/AMPA ionotropic receptor agonist. Sensitizes neurons in hippocampus to depolarization by L-AP6 ("quis" effect).

LIT: The action of natural and synthetic isomers of quisqualic acid at a well-defined glutamatergic synapse: P. Boden, et al.; Brain Res. **385,** 205 (1986) ▪ Agonists and antagonists for metabotropic glutamate receptors: P.L. Ornstein, et al.; Curr. Pharm. Design **1,** 355 (1995) ▪ Pharmacological agents acting at subtypes of metabotropic glutamate receptors: D.D. Schoepp, et al.; Neuropharmacology **38,** 1431 (1999) ▪ L-Quisqualic acid transport into hippocampal neurons by a cystine-sensitive carrier is required for the induction of quisqualate sensitization: L.A. Chase, et al.; Neuroscience **106,** 287 (2001) ▪ Ionotropic and metabotropic glutamate receptor structure and pharmacology: J.N. Kew and J.A. Kemp; Psychopharmacology (Berl.) **179,** 4 (2005)



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14-3-3 – A Multifunctional Signalling Protein

14-3-3 proteins constitute an evolutionarily conserved family of regulatory molecules found in nearly every species. They were identified and received their name in 1967 during a classification of bovine brain proteins. Members of this family modulate the action of target proteins by mechanisms such as sequestration, re-localisation and conformational alterations. Interactions take place in a phosphorylation–dependent manner and affect diverse targets such as various kinases, receptors, enzymes, and structural and cytoskeletal proteins. 14-3-3 proteins play an important role in a wide range of cellular processes such as cell cycling, transcriptional control, signal transduction, intracellular trafficking, and regulating ion channels.

The mammalian family of 14-3-3 proteins consists of seven isoforms (α, ε, γ, η, θ, δ, ζ) encoded by distinct genes. The monomers of these isoforms form active U-shaped dimers of approx. 30kDa. 14-3-3 proteins are known to bind most often to the classical consensus motifs RSX-pSXP and RXY/FXpSXP. Recently, a third motif has been assigned to pS/T [X(1-2)]-COOH.

Because 14-3-3 proteins have multiple targets for binding, they are suspected to play a crucial role in diverse clinical manifestations such as cancer or neurological disorders. The σ-isoform of 14-3-3 appears to be a tumor suppressor by interacting with p53 [1, 2]. In the nervous system several implications of 14-3-3 proteins have been reported. 14-3-3ε is always deleted on one chromosome in patients with a rare, but severe brain disorder called Miller-Dieker syndrome (MDS). The important role of 14-3-3ε has been explained by its protective effect on a protein called NUDEL, which is important in neuronal migration [3]. Several isoforms of 14-3-3 have been reported to mediate the neurotoxicity of a protein called ataxin-1 in spinocerebellar ataxia type 1 [4]. Different isoforms of 14-3-3 are detectable in the cerebrospinal fluid of patients of various neurological disorders like Creuzfeldt-Jakob's disease (CJD), and cattle with bovine spongiform encephalopathy (BSE). Whether 14-3-3 proteins assemble specifically in lesions and protein aggregates within the brain, and to what extent they may have direct influence on neurological disorders like CJD or Alzheimer`s disease remains a matter of debate.

LIT: [1] 14-3-3 sigma positively regulates p53 and suppresses tumor growth: H. Y. Yang, et al.; Mol. Cell Biol. **23,** 7096 (2003) ▪ **[2]** Efp targets 14-3-3 sigma for proteolysis and promotes breast tumour growth: T. Urano, et al.; Nature **417,** 871 (2002) ▪ **[3]** 14-3-3epsilon is important for neuronal migration by binding to NUDEL: a molecular explanation for Miller-Dieker syndrome: K. Toyo-oka, et al.; Nat. Genet. **34,** 274 (2003) ▪ **[4]** Interaction of Akt-phosphorylated ataxin-1 with 14-3-3 mediates neurodegeneration in spinocerebellar ataxia type 1: H. K. Chen, et al.; Cell **113,** 457 (2003)

Selected Review Articles

14-3-3 proteins in the nervous system: D. Berg, et al.; Nat. Rev. Neurosci. **4,** 752 (2003) ▪ The 14-3-3 cancer connection: H. Hermeking; Nat. Rev. Cancer **3,** 931 (2003) ▪ Dynamic interactions between 14-3-3 proteins and phosphoproteins regulate diverse cellular processes: C. Mackintosh; Biochem. J. **381,** 329 (2004) ▪ 14-3-3 proteins: regulators of numerous eukaryotic proteins: G. P. van Heusden; IUBMB Life **57,** 623 (2005) ▪ C-terminal binding: an expanded repertoire and function of 14-3-3 proteins: B. Coblitz, et al.; FEBS Lett. **580,** 1531 (2006)

Neurological Disorders	*Isoform*	*Proposed Function and Comments*
Alzheimer's disease	ζ (β *in vitro*)	Found in NFTs; binds Tau; interaction with Tau might facilitate aberrant Tau phosphorylation
Parkinson's disease	ε, γ, θ, ζ	Found in Lewy bodies; binds α-synuclein; association with α-synuclein might sequester 14-3-3 and inhibit its anti-apoptotic function
Spinocerebellar ataxia type 1	β, ε, γ, η, ζ	Binds ataxin-1; 14-3-3 binding might stabilize and slow the degradation of pathogenic polyglutamine forms of ataxin-1
Miller-Dieker syndrome	ε	Gene encoding 14-3-3ε is deleted in MDS; loss might result in dephosphorylation of NUDEL, mislocalization of the LIS1 complex and reduced cytoplasmic dynein function
Creutzfeldt-Jakob's disease	β, ε, γ, η	No function indicated but found in patients' CSF

Neoplastic Disorders	*Isoform*	*Proposed Function and Comments*
Epithelial cancers (breast, gastric, others)	σ	4-3-3σ levels are reduced/absent due to promoter methylation; binds Cdks and p53; participates in G2/M checkpoint control
Tuberous sclerosis complex	β, γ, ζ (others?)	Binds TSC2; relieves inhibition of mTOR signalling by negatively regulating TSC1/TSC2 complex function

TABLE: Involvement of 14-3-3 in human diseases. Adapted from: Unlocking the code of 14-3-3: M. K. Dougherty & D. K. Morrison; J. Cell Sci. **117,** 1875 (2004)

Product No.	Name	Antigen Specificity	Source	Species Specificity	Application	Size	
ALX-215-030-R100	**PAb to 14-3-3**	Pan	Rabbit	Human, mouse, rat, bovine, sheep, chicken	WB, IHC, IP	100 µl	
ALX-215-021-R100	**PAb to 14-3-3**β	Beta isoform	Rabbit	Human, mouse, rat, bovine, sheep	WB, IHC, ELISA	100 µl	
ALX-215-026-R100	**PAb to 14-3-3**β/ζ **(pSer^{185})**	Beta and zeta isoform (pSer^{185})	Sheep	Human, mouse, rat, bovine, sheep, rabbit	WB	100 µl	
ALX-215-022-R100	**PAb to 14-3-3**ε **(CT)**	Epsilon (C-terminus) isoform	Rabbit	Human, mouse, rat, bovine, sheep, rabbit, chicken	WB, IHC, ELISA	100 µl	
ALX-215-025-R100	**PAb to 14-3-3**ε **(NT)**	Epsilon (N-terminus) isoform	Rabbit	Human, mouse, rat, bovine, sheep, rabbit, chicken	WB, IHC, ELISA	100 µl	
ALX-215-023-R100	**PAb to 14-3-3**η	Eta isoform	Rabbit	Human, mouse, rat, bovine, sheep, chicken	WB, IHC	100 µl	
ALX-215-024-R100	**PAb to 14-3-3**γ	Gamma isoform	Rabbit	Human, mouse, rat, bovine, sheep, chicken	WB, IHC, ELISA	100 µl	
ALX-215-027-R100	**PAb to 14-3-3**σ	Sigma isoform	Rabbit	Human, mouse, rat, bovine, sheep, rabbit, chicken	WB	100 µl	
ALX-215-028-R100	**PAb to 14-3-3**τ/θ	Tau/theta isoform	Rabbit	Human, mouse, rat, bovine, sheep, chicken	WB, IHC, ELISA	100 µl	
ALX-215-029-R100	**PAb to 14-3-3**ζ	Zeta isoform	Rabbit	Human, mouse, rat, bovine, sheep, chicken	WB, IHC, ELISA	100 µl	

Neurobiology Antibodies for Alzheimer's Disease Research

Presenilin Antibodies

MAb to Presenilin 1 (APS 11)
ALX-804-554-C200 200 µg

CLONE: APS 11. **ISOTYPE:** Mouse IgG1. **IMMUNOGEN:** Synthetic peptide corresponding to aa 21-34 (CH^{21}LSNTVRSQNDNRE^{34}) of N-terminal human presenilin 1. **SPECIFICITY:** Recognizes human, rat, mouse and primate presenilin 1. Detects a band of ~28kDa by Western blot. Does not cross-react with presenilin 2. **APPLICATION:** ELISA, IHC (PS), ICC, WB.

LIT: see ALX-804-556

MAb to Presenilin 1 (APS 18)
ALX-804-555-C200 200 µg

CLONE: APS 18. **ISOTYPE:** Mouse IgG1. **IMMUNOGEN:** Synthetic peptide corresponding to aa 313-334 (S^{313}KYNAESTERESQDTVAENDDG^{334}) of C-terminal human presenilin 1. **SPECIFICITY:** Recognizes human, rat, mouse and primate presenilin 1. Detects a band of ~18kDa (C-terminal fragment) and ~46kDa (full-length) presenilin 1 by Western blot. Does not cross-react with presenilin 2. **APPLICATION:** ELISA, ICC, WB.

LIT: see ALX-804-557

PAb to Presenilin 1 (human)
SIG-9360-02 200 µl

From rabbit. **IMMUNOGEN:** Synthetic peptide (TELPAPLSYFNRKC) conjugated to KLH. **SPECIFICITY:** Recognizes human presenilin 1. **APPLICATION:** IP, WB.

LIT: Increased amyloid-beta42(43) in brains of mice expressing mutant presenilin 1: K. Duff, et al.; Nature **383,** 710 (1996) ▪ Presenilins and Alzheimer's disease: the role of A beta 42: C.B. Eckman; J. Neural. Transm. Suppl. **53,** 181 (1998) ▪ A novel gamma -secretase assay based on detection of the putative C-terminal fragmeNT-gamma of amyloid beta protein precursor: I. Pinnix, et al.; J. Biol. Chem. **276,** 481 (2001) ▪ The Role of presenilins in gamma-secretase activity: M.S. Wolfe & C. Haass; J. Biol. Chem. **276,** 5413 (2001)

PAb to Presenilin 1 (human)
ALX-210-562-C100 100 µg

From chicken. **IMMUNOGEN:** Synthetic peptides corresponding to aa 311-322 (K^{311}NSKYNAESTER^{322}) and aa 342-353 (E^{342}AQRDSHLGPHR^{353}) of human presenilin 1. **SPECIFICITY:** Recognizes human, mouse and rat presenilin 1. Detects a band of ~66kDa by Western blot. **APPLICATION:** WB.

MAb to Presenilin 2 (APS 21)
ALX-804-556-C200 200 µg

CLONE: APS 21. **ISOTYPE:** Mouse IgG1. **IMMUNOGEN:** Synthetic peptide corresponding to aa 31-56 (C^{31}QEGRQGPEDGENTA^{45}) of N-terminal human presenilin 2. **SPECIFICITY:** Recognizes human, mouse, rat and monkey presenilin 2. Detects a band of ~28kDa (N-terminal fragment) and ~45kDa (full-length) presenilin 2 by Western blot. Does not cross-react with presenilin 1. **APPLICATION:** ELISA, ICC, WB.

LIT: Analysis of presenilin 1 and presenilin 2 expression and processing by newly developed monoclonal antibodies: A. Diehlmann, et al.; J. Neurosci. Res. **56,** 405 (1999)

MAb to Presenilin 2 (APS 26)
ALX-804-557-C200 200 µg

CLONE: APS 26. **ISOTYPE:** Mouse IgG1. **IMMUNOGEN:** Synthetic peptide corresponding to aa 317-334 (CL^{317}PYDPEMEEDSYDSFGEP^{334}) of C-terminal human presenilin 2. **SPECIFICITY:** Recognizes human, mouse, rat and primate presenilin 2. Detects a band of ~20kDa (C-terminal fragment) and ~45kDa (full-length) presenilin 2 by Western blot. Does not cross-react with presenilin 1. **APPLICATION:** ELISA, ICC, WB.

LIT: Abrogation of the presenilin 1/beta-catenin interaction and preservation of the heterodimeric presenilin 1 complex following caspase activation: G. Tesco, et al.; J. Biol. Chem. **273,** 33909 (1998) ▪ Analysis of presenilin 1 and presenilin 2 expression and processing by newly developed monoclonal antibodies: A. Diehlmann, et al.; J. Neurosci. Res. **56,** 405 (1999)

PAb to Presenilin 2
ALX-210-563-C100 100 µg

From chicken. **IMMUNOGEN:** Synthetic peptides corresponding to aa 319-330 (Y^{319}DPENEEDSYDS^{330}) and aa 349-360 (G^{349}EELEEEEERGV^{360}) of human presenilin 2. **SPECIFICITY:** Recognizes human, mouse and rat presenilin 2. Detects a band of ~66kDa by Western blot. **APPLICATION:** WB.

β-Amyloid Antibodies & Kits

Gold Standards against β-Amyloid

MAb to β-Amyloid (human) (1E11)
SIG-9110-02 200 µl

CLONE: 1E11. **ISOTYPE:** Mouse IgG1. **IMMUNOGEN:** Synthetic peptide corresponding to aa 1-24 (N^{1}AEFRHDSGYQVHHQKLVFFAEDV^{24}) of human β-amyloid. **SPECIFICITY:** Recognizes the N-terminal region (aa 1-8) of human β-amyloid. **APPLICATION:** ELISA, IHC (PS), IP, WB.

LIT: Human choroid plexus is an uniquely involved area of the brain in amyloidosis: a histochemical, immunohistochemical and ultrastructural study: A. Sasaki, et al.; Brain Res. **755,** 193 (1997) ▪ For a comprehensive bibliography please visit our website.

MAb to β-Amyloid (human) (4G8)
SIG-9200-02 Ascites 200 µl
SIG-9220-02 Purified 200 µl
SIG-9240-02 Biotin 200 µl

CLONE: 4G8. **ISOTYPE:** Mouse IgG2b. **IMMUNOGEN:** Synthetic peptide corresponding to aa 17-24 of human β-amyloid. **SPECIFICITY:** Recognizes aa17-24 of human β-amyloid. **APPLICATION:** ELISA, IHC (PS), IP, WB.

LIT: Production and characterization of monoclonal antibodies reactive to synthetic cerebrovascular amyloid peptide: K.S. Kim, et al.; Neurosci. Res. Commun. **2,** 121 (1988) ▪ For a comprehensive bibliography please visit our website.

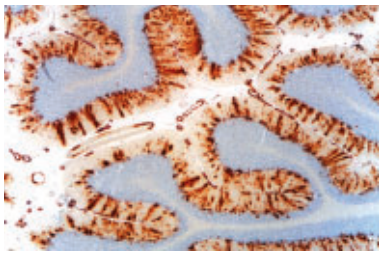

FIGURE: Human cerebellum stained with anti-β-amyloid (human) MAb (4G8), Prod. No. SIG-9200.

MAb to β-Amyloid (human) (6E10)
SIG-9300-02 Ascites 200 µl
SIG-9320-02 Purified 200 µl
SIG-9340-02 Biotin 200 µl

CLONE: 6E10. **ISOTYPE:** Mouse IgG1. **IMMUNOGEN:** Synthetic peptide corresponding to aa 1-17 of human β-amyloid. **SPECIFICITY:** Recognizes aa 1-17 of human β-amyloid. **APPLICATION:** ELISA, IHC (PS), IP, WB.

LIT: see Prod. No. SIG-9200-02.

MAb to β-Amyloid (human) (NT) (19H11)
NT-0084-100 100 µg
NT-0084-100B Biotin 100 µg

CLONE: 19H11. **ISOTYPE:** Mouse IgG1. **IMMUNOGEN:** Synthetic peptide corresponding to a portion of N-terminal human β-amyloid. **SPECIFICITY:** Recognizes N-terminal human β-amyloid. **APPLICATION:** ELISA, ICC, WB.

PAb to β-Amyloid (rodent)
SIG-9153-005 50 µg
SIG-9154-005 Biotin 50 µg

From rabbit. **IMMUNOGEN:** Rodent β-amyloid peptide (aa 3-16). **SPECIFICITY:** Recognizes all isoforms of rodent β-amyloid. **APPLICATION:** ELISA, IHC, WB.

MAb to β-Amyloid (1-40) (CT) (human) (5C3)
NT-0060-100 100 µg
NT-0060-100B Biotin 100 µg
NT-0060-100F FITC 100 µg

CLONE: 5C3. **ISOTYPE:** Mouse IgG1. **IMMUNOGEN:** Synthetic peptide corresponding to aa 1-40 of C-terminal human β-amyloid. **SPECIFICITY:** Recognizes the C-terminus of human β-amyloid (aa 1-40 isoform). Does not cross-react with β-amyloid (aa 1-42 isoform). **APPLICATION:** ELISA, ICC, WB.

MAb to β-Amyloid (1-42) (human) (CT) (8G7)
NT-0061-100 100 µg
NT-0061-100B Biotin 100 µg
NT-0061-100F FITC 100 µg

CLONE: 8G7. **ISOTYPE:** Mouse IgG1. **IMMUNOGEN:** Synthetic peptide corresponding to aa 1-42 of C-terminal human β-amyloid. **SPECIFICITY:** Recognizes the C-terminus of human β-amyloid (aa 1-42 isoform). Does not cross-react with β-amyloid (aa 1-40 isoform). **APPLICATION:** ELISA, ICC, WB.

PAb to β-Amyloid (1-40) (human)
SIG-9130-005 50 µg

From rabbit. **IMMUNOGEN:** Synthetic peptide corresponding to aa 32-40 of human β-amyloid. **SPECIFICITY:** Recognizes C-terminal human β-amyloid 1-40 isoform. Does not cross-react with β-amyloid 1-42 isoform or amyloid precursor protein (APP). **APPLICATION:** ELISA, IHC, WB.

LIT: Quantification of sub-femtomole amounts of Alzheimer amyloid beta peptides: A. Potempska, et al.; Amyloid **6,** 14 (1999) ▪ For a comprehensive bibliography please visit our website.

Product Highlight

NEW PAb to sAPPβ (human)
SIG-9138-005 50 µg

From rabbit. **SPECIFICITY:** Recognizes the soluble fragment of β-secretase cleaved N-terminus of human amyloid precursor protein (APP). Weakly cross-reacts with sAPPα or full length APP. **APPLICATION:** ELISA.

Kits

β-Amyloid (1-40) ELISA Kit
SIG-8940 1 Kit

The most sensitive method for measuring the 1-40 isomer of human β-amyloid in cerebrospinal fluid, plasma and brain tissue. Does not cross-react with the 1-42 isomer. **SENSITIVITY:** 15pg/ml.

β-Amyloid (1-42) ELISA Kit
SIG-8942 1 Kit

The most sensitive method for measuring the 1-42 isomer of human β-amyloid in cerebrospinal fluid, plasma and brain tissue. Does not cross-react with the 1-40 isomer. **SENSITIVITY:** 25-30pg/ml.

For a comprehensive overview on β-Amyloid Products please visit

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Phosphorylated NMDA Receptor Antibodies

PAb to NMDA Receptor (NR2A Subunit) (phosphorylated) (pTyr^{1387})

SIG-9061-50 50 µg

From rabbit. **IMMUNOGEN:** Synthetic peptide corresponding to aa 1382-1399 (C^{1382}PSDPpYKHSLPSQAVNDS^{1399}) of mouse NMDA receptor (NR2A subunit) phosphorylated at Tyr^{1387}. **SPECIFICITY:** Recognizes mouse and rat phosphorylated NMDA receptor NR2A subunit. Does not cross-react with non-phosphorylated NR2A subunit or with any other NMDA receptor subunit. **APPLICATION:** IHC (PS), WB.

PAb to NMDA Receptor (NR2B Subunit) (phosphorylated) (pTyr^{1472})

SIG-9063-50 50 µg

From rabbit. **IMMUNOGEN:** Synthetic peptide corresponding to aa 1467-1478 (S^{1467}NGHVpYEKLSSI^{1478}) of mouse NMDA receptor (NR2B subunit) phosphorylated at Tyr^{1472}. **SPECIFICITY:** Recognizes mouse and rat phosphorylated NMDA receptor NR2B subunit. Does not cross-react with non-phosphorylated NR2B subunit or with any other NMDA receptor subunit. **APPLICATION:** WB.

LIT: Expression of polyglutamine-expanded huntingtin induces tyrosine phosphorylation of N-methyl-D-aspartate receptors: C. Song, et al.; J. Biol. Chem. **278,** 33364 (2003)

Neurobiology Antibodies

High Quality Gephyrin Antibody

PAb to Gephyrin

ALX-210-400-R050 50 µl

From rabbit. **IMMUNOGEN:** Recombinant N-terminal domain corresponding to aa 1-175 of human gephyrin. **SPECIFICITY:** Recognizes different splice forms of human, mouse and rat gephyrin in organs (brain, liver) and cell cultures. **APPLICATION:** IP, WB.

LIT: A mutation in the gene for the neurotransmitter receptor-clustering protein gephyrin causes a novel form of molybdenum cofactor deficiency: J. Reiss, et al.; Am. J. Hum. Genet. **68,** 208 (2001)

Endothelin A Receptor Antibody

PAb to Endothelin A Receptor

ALX-210-507A-C250 250 µg

From sheep. **IMMUNOGEN:** Synthetic peptide corresponding to aa 410-422 (Q^{410}EQNHNTERSSHK^{422}) of C-terminal rat ET_A-receptor (endothelin A receptor). **SPECIFICITY:** Recognizes an epitope on the cytoplasmic side of human, mouse and rat ET_A-receptor. Detects bands of 34-52kDa. Does not block the binding of endothelins to the receptor.

LIT: Endothelin-1-, endothelin-A-, and endothelin-B-receptor expression is correlated with vascular endothelial growth factor expression and angiogenesis in breast cancer: P. Wulfing, et al.; Clin. Cancer Res. **10,** 2393 (2004)

NEW Shc/p66 Antibody

MAb to Shc/p66 (phosphorylated) (pSer^{36}) (6E10)

NT-0094-100 100 µg

CLONE: 6E10. **ISOTYPE:** Mouse IgG1. **IMMUNOGEN:** Synthetic peptide corresponding to aa 33-39 (E^{33}LPpSPSA^{39}) of shc/p66 phosphorylated at Ser^{36}. **SPECIFICITY:** Recognizes human and mouse shc/p66 phosphorylated at Ser^{36}. **APPLICATION:** ELISA, WB.

α-Synuclein Antibodies

NEW

MAb to α-Synuclein (human) (4B12)

SIG-9730-02 200 µl

CLONE: 4B12. **ISOTYPE:** Mouse IgG1. **IMMUNOGEN:** Purified human α-synuclein produced in *E. coli*. **SPECIFICITY:** Recognizes human α-synuclein. Does not cross-react neither with mouse α-synuclein nor with β- or γ-synuclein. **APPLICATION:** ELISA, IHC (FS, PS), ICC, WB.

LIT: Stains for the differential diagnosis of degenerative dementias: D.G. Munoz; Biotech. Histochem. **74,** 311 (1999) ▪ For a comprehensive bibliography please visit our website.

MAb to α-Synuclein (4D6)

SIG-9720-02 200 µl

CLONE: 4D6. **ISOTYPE:** Mouse IgG1. **IMMUNOGEN:** Purified human α-synuclein produced in *E. coli*. **SPECIFICITY:** Recognizes human, mouse and rat α-synuclein. Does not cross-react with β- or γ-synuclein **APPLICATION:** ELISA, IHC (FS, PS), WB.

LIT: Stains for the differential diagnosis of degenerative dementias: D.G. Munoz; Biotech. Histochem. **74,** 311 (1999) ▪ For a comprehensive bibliography please visit our website.

MAb to α-Synuclein (human) (LB509)

SIG-9725-02 200 µl

CLONE: LB509. **ISOTYPE:** Mouse IgG1. **IMMUNOGEN:** Synthetic peptide corresponding to aa 115-122 of human α-synuclein. **SPECIFICITY:** Recognizes human α-synuclein. Does not react with mouse α-synuclein. **APPLICATION:** ELISA, IHC (FS, PS), WB.

LIT: Epitope mapping of LB509, a monoclonal antibody directed against human alpha-synuclein: R. Jakes, et al.; Neurosci. Lett. **269,** 13 (1999) ▪ Aggregation of alpha-synuclein in the pathogenesis of Parkinson's disease: T. Iwatsubo; J. Neurol. 250 Suppl. **3,** III1 1 (2003)

MAb to α-Synuclein (human) (15G7)

ALX-804-258-LC05 0.5 ml
ALX-804-258-L001 1 ml

CLONE: 15G7. **ISOTYPE:** Rat IgG2a. **IMMUNOGEN:** Synthetic peptide corresponding to aa 116-131 of human α-synuclein. **SPECIFICITY:** Recognizes human α-synuclein. Does not cross-react with mouse α-synuclein or recombinant β- or γ-synuclein. **APPLICATION:** IHC (FS, PS), IP, WB.

LIT: Lipid rafts mediate the synaptic localization of alpha-synuclein: D.L. Fortin, et al.; J. Neurosci. **24,** 6715 (2004) ▪ For a comprehensive bibliography please visit our website.

GPCRs Related Antibodies

NEW

PAb to Ionotropic Glutamate Receptor Kainate 2 [GRIK2] (156-205) (human)

ASB-ARP35340-T200 200 µg

From rabbit. **IMMUNOGEN:** Synthetic peptide corresponding to aa 156-205 of human GRIK2 (ionotropic glutamate receptor kainate 2). **SPECIFICITY:** Recognizes human GRIK2. **APPLICATION:** WB.

PAb to Metabotropic Glutamate Receptor 6 [mGluR6] (human)

ASB-ARP32597-P050 50 µg
ASB-ARP32597-P100 100 µg

From rabbit. **IMMUNOGEN:** Synthetic peptide corresponding to a portion of human mGluR6 (metabotropic glutamate receptor 6). **SPECIFICITY:** Recognizes human mGluR6. **APPLICATION:** WB.

PAb to Serotonin Receptor 3B (human)

[PAb to 5-Hydroxytryptamine Receptor 3B]

ASB-ARP35186-P050 50 µg
ASB-ARP35186-P100 100 µg

From rabbit. **IMMUNOGEN:** Synthetic peptide corresponding to a portion of human 5-HT3B (5-hydroxytryptamine receptor 3B; serotonin receptor 3B). **SPECIFICITY:** Recognizes human 5-HT3B. **APPLICATION:** IHC, WB.

For G Protein Coupled Receptors [GPCRs] see Page 2!

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Latest Insight: ACE2 [Angiotensin-converting Enzyme 2]

NEW

The renin-angiotensin system (RAS) has been implicated in the pathogenesis of pulmonary hypertension and pulmonary fibrosis, both commonly seen in chronic lung diseases such as chronic obstructive lung disease. Recent studies indicate that the RAS also plays a critical role in acute lung diseases, especially acute respiratory distress syndrome (ARDS). ACE2, a close homologue of ACE, functions as a negative regulator of the angiotensin system and was identified as a key receptor for SARS (severe acute respiratory syndrome) coronavirus infections. In the lung, ACE2 protects against acute lung injury in several animal models of ARDS. Increasing ACE2 activity might be a novel approach for the treatment of acute lung failure in several diseases.

Selected Review Article

Angiotensin-converting enzyme 2 protects from severe acute lung failure: Y. Imai, et al.; Nature **436,** 112 (2005) • Angiotensin-converting enzyme 2 in lung diseases: K. Kuba, et al.; Curr. Opin. Pharmacol., (in print) (2006)

ACE2 (human):Fc (human) (rec.)

ALX-201-330-C050 50 µg

Produced in HEK 293 cells. The signal peptide sequence and the extracellular domain of human ACE2 (angiotensin-converting enzyme 2) (aa 1-740) are fused at the C-terminus to the Fc portion of human IgG1.

MAb to ACE2 (human) (AC18F)

ALX-804-715-C050 50 µg

CLONE: AC18F. **ISOTYPE:** Mouse IgG1. **IMMUNOGEN:** Recombinant human ACE2:Fc (angiotensin-converting enzyme 2:Fc). **SPECIFICITY:** Recognizes human ACE2. **APPLICATION:** ELISA, FC, WB.

Antibodies

CovalAb's scientific expertise in designing, manufacturing, and characterizing specific antibodies generates a growing panel of unique products. The following overview describes the latest product additions to CovalAb's innovative product pipeline targeting neurobiology.

Collapsin Response Mediator Proteins [CRMPs]

NEW

The CRMP family consist of 5 members, all of them highly expressed throughout brain development. The proteins are involved in apoptosis/proliferation, cell migration and differentiation. The expression of CRMPs is altered in neurodegenerative diseases and may be of key importance in the physiopathology of the adult nervous system.

PAb to CRMP-1
CVL-PAB0114-1 200 µl

From rabbit. **IMMUNOGEN:** Synthetic peptide corresponding to a portion of C-terminal human CRMP-1 [collapsin response mediator protein 1]. **SPECIFICITY:** Recognizes human, mouse and rat CRMP-1. Does not cross-react with CRMP-2, CRMP-3, CRMP-4 or CRMP-5. **APPLICATION:** IHC, IP, WB.

PAb to CRMP-2
CVL-PAB0115-1 200 µl

From rabbit. **IMMUNOGEN:** Synthetic peptide corresponding to a portion of C-terminal human CRMP-2 [collapsin response mediator protein 2]. **SPECIFICITY:** Recognizes human, mouse and rat CRMP-2. Does not cross-react with CRMP-1, CRMP-3, CRMP-4 or CRMP-5. **APPLICATION:** IHC, IP, WB.

PAb to CRMP-3
CVL-PAB0116-1 200 µl

From rabbit. **IMMUNOGEN:** Synthetic peptide corresponding to a portion of C-terminal human CRMP-3 [collapsin response mediator protein 3]. **SPECIFICITY:** Recognizes human, mouse and rat CRMP-3. Does not cross-react with CRMP-1, CRMP-2, CRMP-4 or CRMP-5. **APPLICATION:** IHC, IP, WB.

PAb to CRMP-4
CVL-PAB0117-1 200 µl

From rabbit. **IMMUNOGEN:** Synthetic peptide corresponding to a portion of C-terminal human CRMP-4 [collapsin response mediator protein 4]. **SPECIFICITY:** Recognizes human, mouse and rat CRMP-4. Does not cross-react with CRMP-1, CRMP-2, CRMP-3 or CRMP-5. **APPLICATION:** IHC, IP, WB.

PAb to CRMP-5
CVL-PAB0118-1 200 µl

From rabbit. **IMMUNOGEN:** Synthetic peptide corresponding to a portion of C-terminal human CRMP-5 [collapsin response mediator protein 5]. **SPECIFICITY:** Recognizes human, mouse and rat CRMP-5. Does not cross-react with CRMP-1, CRMP-2, CRMP-3 or CRMP-4. **APPLICATION:** IHC, IP, WB.

LIT: Ulip/CRMP proteins are recognized by autoantibodies in paraneoplastic neurological syndromes: J. Honnorat, et al.; Eur. J. Neurosci. **11,** 4226 (1999) ▪ Isolation and expression pattern of human Unc-33-like phosphoprotein 6/collapsin response mediator protein 5 (Ulip6/CRMP5): coexistence with Ulip2/CRMP2 in Sema3a- sensitive oligodendrocytes: D. Ricard, et al.; J. Neurosci. **21,** 7203 (2001) ▪ Collapsin response mediator proteins (CRMPs): involvement in nervous system development and adult neurodegenerative disorders: E. Charrier, et al.; Mol. Neurobiol. **28,** 51 (2003) ▪ Involvement of collapsin response mediator proteins in the neurite extension induced by neurotrophins in dorsal root ganglion neurons: T.T. Quach, et al.; Mol. Cell Neurosci. **25,** 433 (2004) ▪ Differential expression of CRMP1, CRMP2A, CRMP2B, and CRMP5 in axons or dendrites of distinct neurons in the mouse brain: S. Bretin, et al.; J. Comp. Neurol. **486,** 1 (2005) ▪ Expression of collapsin response mediator proteins 1, 2 and 5 is differentially regulated in newly generated and mature neurons of the adult olfactory system: A. Veyrac, et al.; Eur. J. Neurosci. **21,** 2635 (2005)

Vesicle-associated Membrane Proteins (VAMPs)

VAMPs are integral membrane proteins, also known as synaptobrevin and localized to the cytoplasmic surface of synaptic vesicles, being a component of a 20S complex implicated in vesicle docking. VAMPs are involved in vesicular transport and neurotransmission.

NEW MAb to TI-VAMP (158.2)
CVL-MAB0051-1 200 µl

CLONE: 158.2. **IMMUNOGEN:** Recombinant TI-VAMP fused to a GST-tag. **SPECIFICITY:** Recognizes human, mouse, rat and dog TI-VAMP [tetanus neurotoxin-insensitive vesicle-associated membrane protein]. **APPLICATION:** IHC, IP, WB.

PAb to VAMP-3 (human)
CVL-PAB0053-1 200 µl

From rabbit. **IMMUNOGEN:** Synthetic peptide corresponding to a portion of N-terminal human VAMP-3 (vesicle-associated membrane protein 3; cellubrevin). **SPECIFICITY:** Recognizes human VAMP-3. Detects a band of ~10kDa by Western blot. Does not cross-react with rat or dog VAMP-3. **APPLICATION:** IHC, WB. **BP:** CVL-PEP0011.

PAb to VAMP-3 (rat)
CVL-PAB0055-1 200 µl

From rabbit. **IMMUNOGEN:** Synthetic peptide corresponding to a portion of N-terminal rat VAMP-3 (vesicle-associated membrane protein; cellubrevin). **SPECIFICITY:** Recognizes rat VAMP-3. Detects a band of ~10kDa by Western blot. Does not cross-react with human or dog VAMP-3. **APPLICATION:** IHC, WB. **BP:** CVL-PEP0012.

PAb to VAMP-4 (human)
CVL-PAB0056-1 200 µl

From rabbit. **IMMUNOGEN:** Synthetic peptide corresponding to a portion of N-terminal human VAMP-4 (vesicle-associated membrane protein 4). **SPECIFICITY:** Recognizes human VAMP-4. Detects a band of ~10kDa by Western blot. **APPLICATION:** IHC, WB. **BP:** CVL-PEP0013.

PAb to VAMP-8
CVL-PAB0054-1 200 µl

From rabbit. **IMMUNOGEN:** Synthetic peptide corresponding to a portion of N-terminal human VAMP-8 (vesicle-associated membrane protein 8; endobrevin). **SPECIFICITY:** Recognizes human, rat and dog VAMP-8. Detects a band of ~10kDa by Western blot. **APPLICATION:** IHC, WB.

Antibodies to PrP

PAb to Prion Protein
CVL-PAB0033-1 200 µl

From rabbit. **IMMUNOGEN:** Synthetic peptide corresponding to a portion of C-terminal bovine prion protein (CD230). **SPECIFICITY:** Recognizes full length prion protein of brain tissue from different species including human, rat, sheep and bovine. **APPLICATION:** IHC, WB.

PAb to Prion Protein (purified)
CVL-PAB0034-1 25 µg

From rabbit. **IMMUNOGEN:** Synthetic peptide corresponding to a portion of C-terminal bovine prion protein (CD230). **SPECIFICITY:** Recognizes full length prion protein of brain tissue from different species including human, rat, sheep and bovine. **APPLICATION:** IHC, WB.

MAb to Prion Protein (4H7)
CVL-MAB0026-1 200 µl

CLONE: 4H7. **ISOTYPE:** Mouse IgG2a. **IMMUNOGEN:** Synthetic peptide corresponding to a portion of C-terminal human prion protein (CD230). **SPECIFICITY:** Recognizes brain-tissue prion protein from various species including human, rat, sheep and bovine. **APPLICATION:** IHC, WB.

Neurobiology Antibodies

PAb to Claudin-11 (rat)
CVL-PAB0020-1 200 µl

From rabbit. **IMMUNOGEN:** Synthetic peptide corresponding to a portion of N-terminal claudin-11. **SPECIFICITY:** Recognizes rat claudin-11. Detects a band of ~22kDa by Western blot. **APPLICATION:** IHC, WB. **BP:** CVL-PEP0006.

PAb to Dopamine
CVL-PAB0026-1 200 µl

From rabbit. **IMMUNOGEN:** Dopamine conjugated to BSA. **SPECIFICITY:** Recognizes free and conjugated dopamine. **APPLICATION:** ELISA.

PAb to SNAP-23 (human)
CVL-PAB0057-1 200 µl

From rabbit. **IMMUNOGEN:** SNAP-23 (synaptosomal-asociated protein-23) fused to a GST-tag. **SPECIFICITY:** Recognizes human SNAP-23. Detects a band of ~27kDa by Western blot. **APPLICATION:** IHC, WB.

PAb to Syntaxin-3
CVL-PAB0052-1 200 µl

From rabbit. **IMMUNOGEN:** Syntaxin-3 fused to a GST-tag. **SPECIFICITY:** Recognizes syntaxin-3 of human and several mammalian species. Detects a band of ~35kDa by Western blot. **APPLICATION:** IHC, WB.

Glutamate Transporter Antibodies

Vesicular Glutamate Transporter [vGLUTs]

Glutamate is the primary excitatory neurotransmitter in the mammalian central nervous system (CNS). Three subtypes of vesicular glutamate transporters (VGLUT1-3) have been identified. VGLU1 and 2 are responsible for the uploading of glutamate into pre-synaptic vesicles and are the first specific markers of glutamatergic neurons. Recently, it was shown that glutamatergic pathways play a key role in Parkinson's disease (PD).

PRODUCT SPECIFIC LIT: Altered expression of vesicular glutamate transporters VGLUT1 and VGLUT2 in Parkinson disease: A. Kashani, et al.; Neurobiol. Aging (2006)

PAb to Vesicular Glutamate Transporter Type 1 (rat)

CVL-PAB0047-1 200 µl

From rabbit. **IMMUNOGEN:** Synthetic peptide corresponding to a portion of C-terminal rat vGLUT1 (vesicular glutamate transporter type 1). **SPECIFICITY:** Recognizes rat vGLUT1. Detects a band of ~55-60kDa by Western blot. Does not cross-react with vGLUT2 and vGLUT3. **APPLICATION:** IHC, WB.

PAb to Vesicular Glutamate Transporter Type 1 (rat) (purified)

CVL-PAB0048-1 25 µg

From rabbit. **IMMUNOGEN:** Synthetic peptide corresponding to a portion of C-terminal vGLUT1 (vesicular glutamate transporter type 1). **SPECIFICITY:** Recognizes rat vGLUT1. Detects a band of ~55-60kDa by Western blot. Does not cross-react with vGLUT2 and vGLUT3. **APPLICATION:** IHC, WB.

PAb to Vesicular Glutamate Transporter Type 2

CVL-PAB0049-1 200 µl

From rabbit. **IMMUNOGEN:** Synthetic peptide corresponding to a portion of C-terminal rat vGLUT2 (vesicular glutamate transporter type 2). **SPECIFICITY:** Recognizes human and rat vGLUT2. Detects a band of ~55-60kDa by Western blot. Does not cross-react with vGLUT1 and vGLUT3. **APPLICATION:** IHC, WB.

PAb to Vesicular Glutamate Transporter Type 2 (purified)

CVL-PAB0050-1 25 µg

From rabbit. **IMMUNOGEN:** Synthetic peptide corresponding to a portion of C-terminal rat vGLUT2 (vesicular glutamate transporter type 2). **SPECIFICITY:** Recognizes human and rat vGLUT2. Detects a band of ~55-60kDa by Western blot. Does not cross-react with vGLUT1 and vGLUT3. **APPLICATION:** IHC, WB.

PAb to Vesicular Glutamate Transporter Type 3 (rat)

CVL-PAB0051-1 200 µl

From rabbit. **IMMUNOGEN:** Synthetic peptide corresponding to a portion of C-terminal vGLUT3 (vesicular glutamate transporter type 3). **SPECIFICITY:** Recognizes rat vGLUT3. Detects a band of ~60-62kDa by Western blot. Does not cross-react with vGLUT1 and vGLUT2. **APPLICATION:** IHC, WB.

Other Antibodies

PAb to GLAST (rat)

CVL-PAB0036-1 200 µl

From rabbit. **IMMUNOGEN:** Synthetic peptide corresponding to a portion of C-terminal rat GLAST (glutamate transporter GLAST). **SPECIFICITY:** Recognizes rat GLAST. **APPLICATION:** FC, IHC, WB. **BP:** CVL-PEP0002.

PAb to GLT-1

CVL-PAB0037-1 200 µl

From rabbit. **IMMUNOGEN:** Synthetic peptide corresponding to a portion of C-terminal rat GLT-1 (glutamate transporter GLT-1). **SPECIFICITY:** Recognizes human and rat GLT-1. **APPLICATION:** FC, IHC, WB. **BP:** CVL-PEP0007.

GABA Transporter Antibodies

PAb to GABA Transporter-1

CVL-PAB0014-1 200 µl

From rabbit. **IMMUNOGEN:** Synthetic peptide corresponding to a portion of C-terminal rat GAT-1 (GABA transporter-1). **SPECIFICITY:** Recognizes human, mouse and rat GAT-1. Detects a band of ~72kDa by Western blot. **APPLICATION:** IHC, WB. **BP:** CVL-PEP0003.

PAb to GABA Transporter-1 (purified)

CVL-PAB0015-1 25 µg

From rabbit. **IMMUNOGEN:** Synthetic peptide corresponding to a portion of C-terminal rat GAT-1 (GABA transporter-1). **SPECIFICITY:** Recognizes human, mouse and rat GAT-1. Detects a band of ~72kDa by Western blot. **APPLICATION:** IHC, WB.

PAb to GABA Transporter-2

CVL-PAB0016-1 200 µl

From rabbit. **IMMUNOGEN:** Synthetic peptide corresponding to a portion of C-terminal rat GAT-2 (GABA transporter-2). **SPECIFICITY:** Recognizes human, mouse and rat GAT-2. **APPLICATION:** IHC, WB. **BP:** CVL-PEP0004.

PAb to GABA Transporter-2 (purified)

CVL-PAB0017-1 25 µg

From rabbit. **IMMUNOGEN:** Synthetic peptide corresponding to a portion of C-terminal rat GAT-2 (GABA transporter-2). **SPECIFICITY:** Recognizes human, mouse and rat GAT-2. **APPLICATION:** IHC, WB.

PAb to GABA Transporter-3

CVL-PAB0018-1 200 µl

From rabbit. **IMMUNOGEN:** Synthetic peptide corresponding to a portion of C-terminal rat GAT-3 (GABA transporter-3). **SPECIFICITY:** Recognizes human, mouse and rat GAT-3. Detects a band of ~74kDa by Western blot. **APPLICATION:** IHC, WB. **BP:** CVL-PEP0005.

PAb to GABA Transporter-3 (purified)

CVL-PAB0019-1 25 µg

From rabbit. **IMMUNOGEN:** Synthetic peptide corresponding to a portion of C-terminal rat GAT-3 (GABA transporter-3). **SPECIFICITY:** Recognizes human, mouse and rat GAT-3. Detects a band of ~74kDa by Western blot. **APPLICATION:** IHC, WB.

High Purity, Full-length Myelin Basic Proteins

Native proteins purified according to a unique purification method by J.A. Määttä, et al. [1,2] guaranteed to be at least 95% pure and essentially salt free. Induce experimental autoimmune encephalomyelitis (EAE). Also excellent substrates for CAM and MAP kinases [3].

LIT: [1] Neurotrophins protect cultured cerebellar granule neurons against the early phase of cell death by a two-component mechanism: M.J. Courtney, et al.; J. Neurosci. **17,** 4201 (1997) **[2]** Detection of myelin basic protein isoforms by organic concentration: J.A. Maatta, et al.; BBRC **238,** 498 (1997) **[3]** Activation of mitogen-activated protein kinases in oligodendrocytes: N.R. Bhat and P. Zhang; J. Neurochem. **66,** 1986 (1996)

NEW Myelin Basic Protein [MBP] (human) (high purity) BULK

ALX-200-606-M001 1 mg

NEW Myelin Basic Protein [MBP] (mouse) (high purity) BULK

ALX-202-075-M001 1 mg

NEW Myelin Basic Protein [MBP] (bovine) (high purity) BULK

ALX-202-076-M001 1 mg
ALX-202-076-M005 5 mg

NEW Myelin Basic Protein [MBP] (87-99) (human, bovine, rat)

H-Val-His-Phe-Phe-Lys-Asn-Ile-Val-Thr-Pro-Arg-Thr-Pro-OH

ALX-162-033-M001 1 mg

Manufactured by EspiKem Srl.

Related Products

Immunodominant Epitopes of Myelin Proteins

Multiple sclerosis (MS) is a complex human autoimmune-type disease with a largely unknown pathogenesis. There are basically three myelin-type proteins with specific antigenic epitopes thought to be involved in MS disease pathogenesis and progression: myelin basic protein (MBP), proteolipid protein (PLP) and myelin oligodendrocyte glycoprotein (MOG). In addition myelin proteins were identified as the disease-causing antigens of the animal model experimental autoimmune encephalomyelitis (EAE). Therefore, immunodominant epitopes of myelin proteins (MBP, PLP, MOG) are useful tools for the characterization of the immune response to myelin antigens in patients with MS as well as for the induction of EAE in susceptible animal strains for studying the role of the autoimmune response in the pathogenesis of the disease.

LIT: Multiple sclerosis: D.A. Hafler, et al.; Immunol. Rev. **204,** 208 (2005) ▪ Immunology of Multiple sclerosis: M. Sospedra and R. Martin; Annu. Rev. Immunol. **23,** 683 (2005)

NEW Myelin Oligodendrocyte Glycoprotein [MOG] (35-55) (mouse, rat)

H-Met-Glu-Val-Gly-Trp-Tyr-Arg-Ser-Pro-Phe-Ser-Arg-Val-Val-His-Leu-Tyr-Arg-Asn-Gly-Lys-OH

ALX-162-030-MC05 0.5 mg
ALX-162-030-M001 1 mg

LIT: Neurosphere-derived multipotent precursors promote neuroprotection by an immunomodulatory mechanism: S. Pluchino, et al.; Nature **266,** 436 (2005)

NEW Myelin Proteolipid Protein [PLP] (139-151) (human, bovine, dog, mouse, rat)

H-His-Cys-Leu-Gly-Lys-Trp-Leu-Gly-His-Pro-Asp-Lys-Phe-OH

ALX-162-031-M001 1 mg

LIT: Neurosphere-derived multipotent precursors promote neuroprotection by an immunomodulatory mechanism: S. Pluchino, et al.; Nature **266,** 436 (2005)

NEW [Ser^{140}]-Myelin Proteolipid Protein [PLP] (139-151) (human, bovine, dog, mouse, rat)

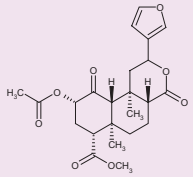
H-His-Ser-Leu-Gly-Lys-Trp-Leu-Gly-His-Pro-Asp-Lys-Phe-OH

ALX-162-032-M001 1 mg

LIT: Identification of an encephalitogenic determinant of myelin proteolipid protein for SJL mice: V.K. Tuohy, et al.; J. Immunol. **142,** 1523 (1989)

These three products are manufactured by EspiKem Srl.

Potent κ-Opioid Agonist



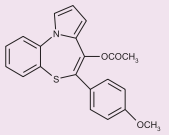
Salvinorin A

ALX-350-126-M001 1 mg
ALX-350-126-M005 5 mg

Isolated from *Salvia divinorum*. Potent naturally occuring non-nitrogenous specific κ-opioid agonist (K_i=4.3-16nM). Shows no action at the 5-HT_{2A} serotonin receptor and other receptors, transporters and ion channels.

LIT: Salvinorin A: a potent naturally occurring non-nitrogenous kappa opioid selective agonist: B.L. Roth, et al.; PNAS **99,** 11934 (2002) ▪ Salvinorin A, an active component of the hallucinogenic sage salvia divinorum is a highly efficacious kappa-opioid receptor agonist: structural and functional considerations: C. Chavkin, et al.; J. Pharmacol. Exp. Ther. **308,** 1197 (2004) ▪ Salvinorin A: a novel and highly selective kappa-opioid receptor agonist: F. Yan, et al.; Life Sci. **75,** 2615 (2004) (Review) ▪ A unique binding epitope for salvinorin A, a non-nitrogenous kappa opioid receptor agonist: B. E. Kane, et al.; FEBS J. **273,** 1966 (2006)

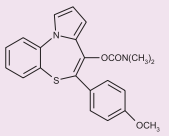
Specific Ligands for Mitochondrial Benzodiazepine Receptors



LIT: Novel ligands specific for mitochondrial benzodiazepine receptors: 6-arylpyrrolo[2,1-d][1,5]benzothiazepine derivatives. Synthesis, structure-activity relationships, and molecular modeling studies: I. Fiorini, et al.; J. Med. Chem. **37,** 1427 (1994)

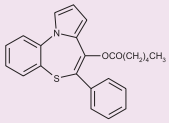
NF 49

ALX-550-114-M001 1 mg
ALX-550-114-M005 5 mg



NF 51

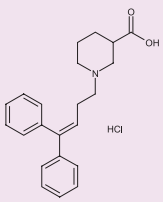
ALX-550-113-M001 1 mg
ALX-550-113-M005 5 mg



NF 115 BULK

ALX-550-112-M001 1 mg
ALX-550-112-M005 5 mg

Potent GABA Uptake Inhibitor



SKF 89976A . HCl

[1-(4,4-Diphenyl-3-butenyl)-3-piperidinecarboxylic acid . HCl]

ALX-550-406-M005 5 mg
ALX-550-406-M025 25 mg

Potent GABA uptake inhibitor. Selective for GABA transporter GAT-1 (human GAT-1 IC_{50}=0.13μM, rat GAT-1 IC_{50}=550μM, human GAT-3 IC_{50}=944μM and human BGT-1 IC_{50}=7210μM). Passes the blood-brain barrier after systemic administration. Active *in vivo.*

LIT: Orally active and potent inhibitors of gamma-aminobutyric acid uptake: F.E. Ali, et al.; J. Med. Chem. **28,** 653 (1985) ▪ Tiagabine, SK&F 89976-A, CI-966, and NNC-711 are selective for the cloned GABA transporter GAT-1: L.A. Borden, et al.; Eur. J. Pharmacol. **269,** 219 (1994)

Hedgehog (Hh) Pathway Modulators

The signalling molecule Hedgehog (Hh) is involved in several processes of central nervous system development. Recent reports indicate that Hh expression plays a role in certain pathological conditions in adult brain, including multiple sclerosis. Smoothened (Smo), a distant relative of G protein coupled receptors, mediates Hh signalling during embryonic development and can initiate or transmit ligand-independent pathway activation in tumorigenesis.

LIT: The Hedgehog response network: sensors, switches, and routers: L. Lum & P.A. Beachy; Science **304,** 1755 (2004) ▪ Hedgehog signaling: measuring ligand concentrations with receptor ratios: J. Briscoe; Curr. Biol. **14,** R889 (2004)

SAG

ALX-270-426-M001 1 mg

Potent agonist of Hedgehog (Hh) signalling by activating the Smoothened (Smo) protein function.

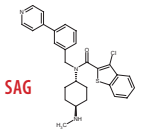
LIT: Small molecule modulation of Smoothened activity: J.K. Chen, et al.; PNAS **99,** 14071 (2002) ▪ Small-molecule modulators of Hedgehog signaling: identification and characterization of Smoothened agonists and antagonists: M. Frank-Kamenetsky, et al.; J. Biol. **1,** 10 (2002) ▪ Activity-dependent internalization of smoothened mediated by beta-arrestin 2 and GRK2: W. Chen, et al.; Science **306,** 2257 (2004)

NEW SANT-2

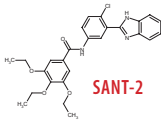
ALX-270-436-M001 1 mg

Cell permeable antagonist of the Smoothened (Smo) protein function. Inhibitor of SAG (Prod. No. ALX-270-426) activity. Chemical tool to study the Hedgehog (Hh) signalling pathway and to explore therapeutic uses for inhibitors of Smo.

LIT: Small molecule modulation of Smoothened activity: J.K. Chen, et al.; PNAS **99,** 14071 (2002)



SAG



SANT-2

Matriptase [Membrane-type Serine Protease 1] & Related Products

The type II transmembrane serine proteases (TTSPs) are an emerging class of cell surface proteolytic enzymes. Matriptase, one of the most extensively studied member of this family, has the broadest expression pattern of all the TTSPs, being detected in a wide range of human tissues.

Matriptase (human) (rec.)

ALX-201-246-U125 125 U

Produced in *E. coli*. Recombinant human membrane-type serine protease 1 (matriptase) (aa 596-855) is fused at the N-terminus to a His-tag. **MW:** ~25kDa. **PURITY:** >98% (SDS-PAGE). **QUANTITY:** ~125 U/vial. One unit is defined as the amount of enzyme that releases 1nmol of AMC per min. at 37°C when incubated with 50 μM of Boc-Gln-Ala-Arg-AMC.

LIT: Reverse biochemistry: Use of macromolecular protease inhibitors to dissect complex biological processes and identify a membrane-type serine protease in epithelial cancer and normal tissue: T. Takeuchi, et al.; PNAS **96,** 11054 (1999)

PAb to Matriptase (800-855) (human) (BL863)

BET-A300-221A 0.1 mg

From rabbit. **IMMUNOGEN:** Synthetic peptide corresponding to aa 800-855 of C-terminal human membrane-type serine protease 1 (matriptase). **SPECIFICITY:** Recognizes human matriptase. **APPLICATION:** IP, WB. **BP:** BET-BP300-221.

Latest Insight

A. Désilets, et al. describe the inhibition of human matriptase by eglin C variants.

LIT: Inhibition of human matriptase by eglin c variants: A. Desilets, et al.; FEBS Lett. **580,** 2227 (2006)

N-Acetyl-eglin C (rec.)

ALX-201-006-MC01 0.1 mg
ALX-201-006-MC05 0.5 mg
ALX-201-006-M001 1 mg

Cell Permeable Labelled Inhibitor of Cysteine Proteases

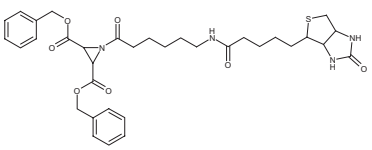
bADA

[Dibenzyl-1-biotin-6-aminohexanoyl-aziridin-2,3-dicarboxylate]

ALX-620-080-M002 2 mg

Irreversible, cell permeable, biotin-labelled inhibitor of cysteine proteases.

LIT: Synthesis and antiplasmodial activity of a cysteine protease-inhibiting biotinylated aziridine-2,3-dicarboxylate: C. Gelhaus, et al.; Biol. Chem. **385,** 435 (2004) ▪ Blocking effect of a biotinylated protease inhibitor on the egress of Plasmodium falciparum merozoites from infected red blood cells: C. Gelhaus, et al.; Biol. Chem. **386,** 499 (2005)



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