Mambalgin-1

Novel Peptide Blocker for Acid-Sensing Ion Channels

It is well-established that acid-sensing ion channels (ASICs) are essential regulators/modulators in the sensory peripheral pain pathways, thus making blockers of these channels potential analgesic reagents for research of pain management/treatment. The disulfide rich peptide toxins, psalmotoxin 1 (Code 4435-s) and APETx2 (Code 4472-s), are examples of blockers which target and inhibit ASIC1a and ASIC3, respectively. Very recently, a novel blocker of ASICs called mambalgin-1[1] was isolated from the venom of the black mamba, *Dendroaspis polylepis polylepis*; this 57-residue peptide is stabilized by four disulfide linkages in a **I-III**, **II-IV**, **V-VI**, and **VII-VIII** cysteine arrangement (cysteine numbering from the amino-terminus), which is proposed based on the modeling experiments[1]. Results of the sequence alignment with other snake venom toxins and secondary structure prediction suggest that mambalgin-1 belongs to a member of snake three-finger toxins.

Mambalgin-1

LKCYQHGKVVTCHRDMKFCYHNTGMPFRNL
KLILQGCSSSCSETENNKCCSTDRCNK

The specificity values of blocking expressed ASICs by mambalgin-1 are as follows; **i)** IC_{50} values for human ASICs are 127 nM (homomeric ASIC1a) and 674 nM (heteromeric ASIC1a-2a), and those for rat ASICs are 55 nM (homomeric ASIC1a), 246 nM (heteromeric ASIC1a-2a), 61 nM (heteromeric ASIC1a-2b), 192 nM (homomeric ASIC1b), and 72 nM (heteromeric ASIC1a-1b), **ii)** homomeric ASIC2a and ASIC3-containing channels are not inhibited, and **iii)** TRPV1, Nav1.8, Cav3.2, Kv1.2, P2X2, and 5-HT_{3A} are also unaffected. In addition to these experiments, mambalgin-1 was found to block native ASIC currents in the central nervous system (CNS) and peripheral neurons in mouse. Analgesic effect was the consequence of the central or peripheral injection of mambalgin-1 to mouse (0.34 nmol), which was as potent as that of morphine but insensitive to naloxone.

Mambalgin-1 seems to be an effective pain-killing reagent without adverse effects of morphine, therefore, further experimental research using synthetic mambalgin-1 may help to develop a novel analgesic agent.

Code	Compound	Quantity	Price: Yen
New 4473-s	Mambalgin-1	0.1 mg vial	30,000
4435-s	Psalmotoxin 1	0.1 mg vial	23,000
New 4472-s	APETx2	0.1 mg vial	25,000

Reference: 1) S. Diochot, *et al*., *Nature*, **490**, 552 (2012).

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APETx2 ・ Mambalgin-1

“痛み”関連イオンチャンネルAcid-Sensing Ion Channels（ASICs）

ペプチド性ブロッカー

2種類　新発売 !!

APETx2 は イソギンチャク***Anthopleura elegantissima*** の毒液から単離されたアミノ酸 42 残基からなる分子内に3組のジスルフィド結合を有するペプチドで **ASIC3**（Acid-Sensing Ion Channel 3）**特異的ブロッカー**として報告されました[1]。

Mambalgin-1 はヘビ black mamba (*Dendroaspis polylepis polylepis)*の毒液から単離されたアミノ酸 57 残基からなる分子内に4組のジスルフィド結合を有するペプチドでPsalmotoxin 1やAPETx2とは特異性の異なる**ASICs**（Acid-Sensing Ion Channels）**ブロッカー**として報告されました[2]。

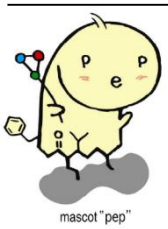
Psalmotoxin 1はクモSouth American Tarantula(*Psalmopoeus cambridgei)*の毒液から単離されたアミノ酸40 残基からなる分子内に3組のジスルフィド結合を有するペプチドで **ASIC1a**（Acid-Sensing Ion Channel 1a）**特異的ブロッカー**として報告[3]された後、当社でも化学合成しこれまでに、好評販売しております。

今後、これら3種類の特異性の異なるASICsペプチド性ブロッカーが、ASICs機能解析の強力なToolとなると期待されます。

文献

1) S. Diochot, *et al., EMBO J.*, **23**, 1516 (2004).
2) S. Diochot, *et al., Nature,* **490**, 552 (2012).
3) P. Escoubas, *et al., J. Biol. Chem.*, **275**, 25116 (2000).

	コード	品名	容量	価格
New	4472-s	APETx2	0.1 mg vial	¥25,000
		Selective Blocker for ASIC3		
New	4473-s	Mambalgin-1	0.1 mg vial	¥30,000
		Analgesic Peptide Targeting to ASICs		
	4435-s	Psalmotoxin 1	0.1 mg vial	¥23,000
		Selective Blocker for ASIC1a		



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