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Biologically Active Peptides

APETx2

Code	Compound			Price:Yen
4472-s New -20℃	**APETx2** **(Sea Anemone, *Anthopleura elegantissima*)** Gly-Thr-Ala-Cys-Ser-Cys-Gly-Asn-Ser-Lys- Gly-Ile-Tyr-Trp-Phe-Tyr-Arg-Pro-Ser-Cys- Pro-Thr-Asp-Arg-Gly-Tyr-Thr-Gly-Ser-Cys- Arg-Tyr-Phe-Leu-Gly-Thr-Cys-Cys-Thr-Pro- Ala-Asp (Reported disulfide bonds between Cys^{4}-Cys^{37}, Cys^{6}-Cys^{30}, Cys^{20}-Cys^{38}) (M.W. 4561.0) $C_{196}H_{280}N_{54}O_{61}S_{6}$ [713544-47-9] Purity ≧99.0% (HPLC)	Vial	0.1 mg	25,000

Selective Blocker of Acid-Sensing Ion Channel, ASIC3

Tissue acidosis is a common feature of many painful conditions. Protons are initially released by injured tissues, and this leads to pain. Acid-sensing ion channels (ASICs) are excitatory cation channels directly gated by extracellular protons, and composed of several isoforms which assemble into functional homo- and heteromeric tetramers. These channels are activated in response to the extracellular pH drop and involved in numerous functions including pain caused by acidosis[1,2]. A specific inhibitor of an individual ASIC is required to discriminate a particular ASIC from others and to understand its function. Psalmotoxin 1 (Code 4435-s) is a peptidic inhibitor specific to homomeric ASIC1a. **APETx2**, another peptidic toxin isolated from the sea anemone *Anthopleura elegantissima*, is classified into the ASIC3-specific inhibitor[3]. **APETx2** is a 42-residue peptide with three disulfide linkages in a I-V, II-IV, and III-VI cysteine arrangement (cysteine numbering from the amino-terminus)[3] and a member of the disulfide-rich all-β-structural family peptides[4].

APETx2 shows a reversible inhibition of ASIC3-evoked peak current in an isoform-dependent manner[3,5]; for rat channels IC_{50} values are 63 nM (homomeric ASIC3), 117 nM (heteromeric ASIC2b-3), and for human channels IC_{50} value is 175 nM (homomeric ASIC3). **APETx2**-elicited functions through ASIC3 inhibition include; **i)** suppression of postoperative[6], acid-induced muscle[7], and inflammatory[7,8] pain and thus exerting analgesic effects in rat and **ii)** increase of insulin resistance and regulation of anxiety in mouse[9], whereas some adverse effects are suggested in association with the blockade of ASIC3[9]. **APETx2** as well as Psalmotoxin 1 are obviously indispensable tools to be used in the research of ASIC-associated pain. Both peptides are available from Peptide Institute, Inc. In addition to these ASIC blocker, novel mambalgin-1 (Code 4473-s) has been listed recently as our items.

1) Z.-G. Xiong, G, Pignataro, M. Li, S.-y. Chang and R.P. Simon, *Curr. Opin. Pharmacol.*, **8**, 25 (2008). (*Review*)
2) E. Deval, X. Gasull, J. Noël, M. Salinas, A. Baron, S. Diochot, and E. Lingueglia, *Pharmacol. Ther.*, **128**, 549 (2010). (*Review; Implication of ASIC3 in Pain*)
3) S. Diochot, A. Baron, L.D. Rash, E. Deval, P. Escoubas, S. Scarzello, M. Salinas, and M. Lazdunski, *EMBO J.*, **23**, 1516 (2004). (*Original; Primary Structure, S-S Bond & Pharmacol.*)
4) B. Chagot, P. Escoubas, S. Diochot, C. Bernard, M. Lazdunski, and H. Darbon, *Protein Sci.*, **14**, 2003 (2005). (*NMR Structure*)
5) S. Diochot, M. Salinas, A. Baron, P. Escoubas, and M. Lazdunski, *Toxicon*, **49**, 271 (2007). (*Pharmacol.*)
6) E. Deval, J. Noël, X. Gasull, A. Delaunay, A. Alloui, V. Friend, A. Eschalier, M. Lazdunski, and E. Lingueglia, *J. Neurosci.*, **31**, 6059 (2011). (*Pharmacol.*)
7) J. Karczewski, R.H. Spencer, V.M. Garsky, A. Liang, M.D. Leitl, M.J. Cato, S.P. Cook, S. Kane and M.O. Urban, *Br. J. Pharmacol.*, **161**, 950 (2010). (*Pharmacol.*)
8) E. Deval, J. Noël, N. Lay, A. Alloui, S. Diochot, V. Friend, M. Jodar, M. Lazdunski, and E. Lingueglia, *EMBO J.*, **27**, 3047 (2008). (*Pharmacol.*)
9) W.-L. Wu, C.-F. Cheng, W.-H. Sun, C.-W. Wong, and C.-C. Chen, *Pharmacol. Ther.*, **134**, 127 (2012). (*Review; Pharmacol.*)

Mambalgin-1

Code	Compound			Price:Yen
4473-s New -20℃	**Mambalgin-1** **(Black Mamba, *Dendroaspis polylepis polylepis*)** Leu-Lys-Cys-Tyr-Gln-His-Gly-Lys-Val-Val- Thr-Cys-His-Arg-Asp-Met-Lys-Phe-Cys-Tyr- His-Asn-Thr-Gly-Met-Pro-Phe-Arg-Asn-Leu- Lys-Leu-Ile-Leu-Gln-Gly-Cys-Ser-Ser-Ser- Cys-Ser-Glu-Thr-Glu-Asn-Asn-Lys-Cys-Cys- Ser-Thr-Asp-Arg-Cys-Asn-Lys (Reported disulfide bonds between Cys^{3}-Cys^{19}, Cys^{12}-Cys^{37}, Cys^{41}-Cys^{49}, and Cys^{50}-Cys^{55}) (M.W. 6554.5) $C_{272}H_{429}N_{85}O_{84}S_{10}$ [1401381-87-0] Purity ≧99.0% including Met (O) analog (≦1.0%) (HPLC)	Vial	0.1 mg	30,000

Analgesic Peptide Targeting to 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. 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 computer modeling experiments and subsequently confirmed by NMR structure analysis[2)]. 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.

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 $5\text{-}HT_{3A}$ 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.

1) S. Diochot, A. Baron, M. Salinas, D. Douguet, S. Scarzello, A.-S. Dabert-Gay, D. Debayle, V. Friend, A. Alloui, M. Lazdunski, and E. Lingueglia, *Nature*, **490**, 552 (2012). (*Original*)
2) M. Pan, Y. He, M. Wen, F. Wu, D. Sun, S. Li, L. Zhang, Y. Li, and C. Tian, *Chem. Commun.*, **50**, 5837 (2014). (*NMR Structure & S-S Bond*)

Code	Compound			Price:Yen
4474-v New -20℃	**Angiotensin A** **[Ala^1]-Angiotensin II** **(Human)** Ala-Arg-Val-Tyr-Ile-His-Pro-Phe (M.W. 1002.2) $C_{49}H_{71}N_{13}O_{10}$ [51833-76-2] Purity ≧99.0% (HPLC)	Vial	0.5 mg	3,000

Novel Form of Angiotensin II

Angiotensin II (Human) (Code 4001-v) is a major component in the renin-angiotensin system and influences many biological functions in the cardiovascular system. A novel angiotensin II-related peptide named **angiotensin A** was identified in human plasma by mass spectrometry[1)]. **Angiotensin A** is similar to angiotensin II, but with Asp-to-Ala substituted at position 1, and is most likely generated from angiotensin II by a decarboxylase. For end-stage renal failure patients, plasma concentration of **angiotensin A** has been found to be higher than that of healthy subjects (5.1-73.6% vs. 2.1-25.2% of the angiotensin II concentration).

Angiotensin A shows a higher affinity to the angiotensin II type 2 (AT_2) receptor than angiotensin II, whereas the affinity of this peptide to the AT_1 is the same as that of angiotensin II. Considering the facts that: **i)** **angiotensin A** elicits lower vasoconstricting activity than angiotensin II in the isolated perfused rat kidney and **ii)** **angiotensin A**-induced hypertensive response is achieved at almost 10 times higher concentration than angiotensin II-induced hypertensive response, along with results from some experiments using receptor-selective antagonists, **angiotensin A** has been shown to be a partial agonist of the AT_{1A} receptor. The ratio of **angiotensin A** versus angiotensin II is relatively large and shown to increase in renal failure patients. Therefore, **angiotensin A** may be essential for evaluating the angiotensin-induced biological functions in humans and other animals. In a Langendorff-prepared heart of a rat, an infusion of **angiotensin A** caused a significant reduction in the coronary flow[2)]. Angiotensin II elicited an increase in the duration of ischemia/reperfusion arrhythmias while **angiotensin A** had no effect on cardiac rhythm during reperfusion[2)].

1) V. Jankowski, R. Vanholder, M. van der Giet, M. Tölle, S. Karadogan, J. Gobom, J. Furkert, A. Oksche, E. Krause, T. N. A. Tran, M. Tepel, M. Schuchardt, H. Schlüter, A. Wiedon, M. Beyermann, M. Bader, M. Todiras, W. Zidek, and J. Jankowski, *Arterioscler. Thromb. Vasc. Biol.*, **27**, 297 (2007). (*Original*)
2) D.C. Coutinho, G. Foureaux, K.D. Rodrigues, R.L. Salles, P.L. Moraes, T.M. Murça, M.L. De Maria, E.R. Gomes, R.A. Santos, S. Guatimosim, and A.J. Ferreira, *J. Renin-Angiotensin-Aldosterone Syst.*, DOI:10.1177/1470320312474856 (*Pharmacol.*)

Code	Compound			Price:Yen
4475-v New -20℃	**Alamandine** **[Ala¹]-Angiotensin (1-7), Angiotensin A (1-7)** **(Human, Rat, Mouse)** Ala-Arg-Val-Tyr-Ile-His-Pro (M.W. 855.00) $C_{40}H_{62}N_{12}O_9$ [1176306-10-7] Purity ≧99.0% (HPLC)	Vial	0.5 mg	3,000

Novel Form of Angiotensin (1-7)

Angiotensin (1-7) (Code 4332-v), which is generated from angiotensin II by the action of angiotensin converting enzyme 2 (ACE2), is an endogenous peptide that shows the opposite effects of angiotensin II, such as vasodilation and antihypertensive activity.

When substituting Ala for Asp at position 1 in angiotensin (1-7), the resulting peptide named **alamandine**, was discovered in early 2013 as a novel peptide of the renin-angiotensin system[1). **Alamandine** is generated through dual pathways: one from angiotensin A (Code 4474-v) by ACE2, and another from angiotensin (1-7) by decarboxylation at the side chain of Asp. **Alamandine** shows similar biological functions to angiotensin (1-7): **i)** vasodilation at nM range, **ii)** a vasopressor effect in SHR (50 μg/kg) by oral administration of β-hydroxypropyl cyclodextrin complex, and **iii)** antifibrosis in rats (50 μg/kg). These functions of **alamandine** are expressed through Mas-related G-protein-coupled receptor member D (MrgD), but not through Mas and angiotensin II type 2 receptors, to which angiotensin (1-7) interacts and exerts its biological activities[2).

The novel endogenous peptide **alamandine** will help understand the physiological roles of angiotensin (1-7) and related peptides more thoroughly and precisely.

1) R.Q. Lautner, D.C. Villela, R.A. Fraga-Silva, N. Silva, T. Verano-Braga, F. Costa-Fraga, J. Jankowski, V. Jankowski, F. Sousa, A. Alzamora, E. Soares, C. Barbosa, F. Kjeldsen, A. Oliveira, J. Braga, S. Savergnini, G. Maia, A.B. Peluso, D. Passos-Silva, A. Ferreira, F. Alves, A. Martins, M. Raizada, R. Paula, D. Motta-Santos, F. Klempin, A. Pimenta, N. Alenina, R. Sinisterra, M. Bader, M.J. Campagnole-Santos, and R.A.S. Santos, *Circ. Res.*, **112**, 1104 (2013). (*Original*)

2) D.C. Villela, D.G. Passos-Silva, and R.A. Santos, *Curr. Opin. Nephrol. Hypertens.*, **23**, 130 (2014). (*Review*)

Code	Compound			Price:Yen
4476-v New -20℃	**[Sar[1], Ile[4,8]]-Angiotensin II** **SII** Sar-Arg-Val-Ile-Ile-His-Pro-Ile (M.W. 918.14) $C_{43}H_{75}N_{13}O_9$ [185461-45-4] Purity ≧99.0% (HPLC)	Vial	0.5 mg	3,000

β-Arrestin Selective Angiotensin II Type 1A Receptor Agonist

It has been discovered that activation of a G-protein-coupled receptor (GPCR) by a ligand follows two distinct signaling pathways: G-protein-dependent and G-protein-independent signaling. In the latter case, downstream signaling is associated with the recruitment of the scaffolding protein β-arrestin. Binding of β-arrestin to the receptor desensitizes the activated receptor, promotes the receptor internalization, and functionally activates the G-protein-independent signaling. Thus, it is possible to segregate the signaling independence from dependency on G-protein by using a specific ligand, "biased agonist". A biased agonist is a ligand involved in the G-protein-independent signaling, whereas it is characterized as an antagonist against the G-protein-mediated functions.

In the renin-angiotensin system (RAS), angiotensin II (Code 4001-v) is a ligand of the angiotensin II type 1A receptor ($AT_{1A}R$) and shows various functional roles such as regulation of blood pressure and water intake. In RAS, the synthetic angiotensin II analog, **[Sar[1],Ile[4,8]]-angiotensin II** (**SII**) is a well-known prototypical biased agonist of $AT_{1A}R$[1)]. Many papers researching **SII** have been published, such as those referenced below[2-5)]. This includes a conflicting one which show **SII** is not a biased agonist, but rather a distinct agonist of AT_1R in a G-protein-dependent manner by using a special experimental protocol[5)]. Biased agonists such as **SII** continuously attract researchers studying RAS because the adverse effect of the parental peptide may be avoided by using biased agonists specifically in the development of the therapeutic agents.

We now are distributing **SII** as one of our catalog items. In addition, we can also assist in the development of a novel biased agonist of angiotensin II by synthesizing the candidate peptide(s) as custom service product(s), even under GMP guidelines.

1) H. Wei, S. Ahn, S.K. Shenoy, S.S. Karnik, L. Hunyady, L.M. Luttrell, and R.J. Lefkowitz, *Proc. Natl. Acad. Sci. U.S.A.*, **100**, 10782 (2003). (*Pharmacol.*)
2) C.M. Godin and S.S.G. Ferguson, *Mini Rev. Med. Chem.*, **12**, 812 (2012). (*Review*)
3) R.T. Kendall, E.G. Strungs, S.M. Rachidi, M.-H. Lee, H.M. El-Shewy, D.K. Luttrell, M.G. Janech, and L.M. Luttrell, *J. Biol. Chem.*, **286**, 19880 (2011). (*Pharmacol.*)
4) P.C. Wilson, M.-H. Lee, K.M. Appleton, H.M. El-Shewy, T.A. Morinelli, Y.K. Peterson, L.M. Luttrell, and A.A. Jaffa, *J. Biol. Chem.*, **288**, 18872 (2013). (*Pharmacol.*)
5) A. Saulière, M. Bellot, H. Paris, C. Denis, F. Finana, J.T. Hansen, M.-F. Altié, M.-H. Seguelas, A. Pathak, J.L. Hansen, J.-M. Sénard, and C. Galés, *Nat. Chem. Biol.*, **8**, 622 (2012). (*Pharmacol.*)

Apelin

Code	Compound			Price:Yen
4478-s New -20℃	**Apelin-36 (Human, 1-16 Amide)** **SCNH2** (Selective Apelin-36 Cutting and Amidation Peptide) **(Human, Simian, Canine)** Leu-Val-Gln-Pro-Arg-Gly-Ser-Arg-Asn-Gly- Pro-Gly-Pro-Trp-Gln-Gly-NH_2 (M.W. 1704.9) $C_{74}H_{117}N_{27}O_{20}$ [1241836-78-1] Purity ≧99.0% (HPLC)	Vial	0.1 mg	5,000

Novel Apelinergic Family Member

When looking at the primary structure of human apelin-36 (Code 4362-s), there are several possible processing sites to produce alternative peptides. Actually, [Pyr^1]-apelin-13 (Code 4361-v) with its multiple biological functions is generated from apelin-36. Both the parental apelin-36 and the processed 13-residue peptide are considered to be a ligand for the APJ-receptor[1)].

Another processed peptide, **Apelin-36 (Human, 1-16 Amide)**, abbreviated as **SCNH2 (selective apelin-36 cutting and amidation peptide)**, was hypothesized, based on the presence of the amidation motif of Gly-Arg-Arg-Lys in apelin-36 and in fact, in early 2013 **SCNH2** was identified as an endogenous peptide[2)]. **SCNH2** shows the similar functions to [Pyr^1]-apelin-13: **i)** mitogenic activity at nM range, **ii)** augmentation of angiogenesis (pM-nM), and **iii)** cell migration and invasion (pM). However, potencies of these activities are higher in **SCNH2** than those of not only [Pyr^1]-apelin-13, but also vascular endothelial growth factor-A. Furthermore, the receptor involved in the activity of **SCNH2** is a pertussis toxin-resistant/chloral toxin-sensitive G protein-coupled receptor (GPCR), indicating that the **SCNH2** receptor is distinct from the APJ GPCR of [Pyr^1]-apelin-13 and apelin-36. Immunohistochemical staining reveals that endogenous **SCNH2** is expressed in human placenta, lung and solid tumor tissue arrays. This novel peptide **SCNH2** may be an essential member in the study in the apelinergic system.

1) K. Tatemoto, M. Hosoya, Y. Habata, R. Fujii, T. Kakegawa, M.X. Zou, Y. Kawamata, S. Fukusumi, S. Hinuma, C. Kitada, T. Kurokawa, H. Onda, and M. Fujino, *Biochem. Biophys. Res. Commun.*, **251**, 471 (1998). (*Apelin and APJ Receptor*)
2) C. Fang, I. Avis, C. Bianco, N. Held, J. Morris, K. Ylaya, S.M. Hewitt, A.C. Aplin, R.F. Nicosia, L.A. Fung, J.D. Lewis, W.G. Stetler-Stevenson, D.S. Salomon, and F. Cuttitta, *Open J. Clin. Diagn.*, **3**, 37 (2013). (*Original & Pharmacol.*)

Catestatin

Code	Compound			Price:Yen
4470-v New -20℃	**Catestatin (Human)** **Chromogranin A (Human, 352-372)** Ser-Ser-Met-Lys-Leu-Ser-Phe-Arg-Ala-Arg-Ala-Tyr-Gly-Phe-Arg-Gly-Pro-Gly-Pro-Gln-Leu (M.W. 2326.7) $C_{104}H_{164}N_{32}O_{27}S$ [197151-46-5] Purity ≧99.0% including Met (O) analog (≦1.0%) (HPLC)	Vial	0.5 mg	16,000

Antimicrobial Peptide / Regulator of Blood Pressure/Cardiac Function

In the primary structure of chromogranin A, a member of the granin family protein, many biologically active peptides are encoded. Among others including chromogranin A (Human, 286-301 Amide) [Code 4214-v], **catestatin (human)** is one of such endogenously processed peptides: **catestatin (human)** is composed of 21 amino acid residues corresponding to (352-372) of mother protein[1). Nowadays, **catestatin (human)** is categorized as a multifunctional peptide although this peptide was originally discovered to be an antagonist against catecholamine secretion[2-4). These functions include: **i)** stimulation of histamine release from mast cells, **ii)** induction of chemotaxis in human monocytes, **iii)** antimicrobial activity against skin pathogens, and **iv)** cardiovascular function such as vasodilation and blood lowering effect.

Catestatin (human) is not the newly identified peptide, but may attract many researchers because review articles have been appeared frequently within several years.

1) D.S. Konecki, U.M. Benedum, H.-H. Gerdes, and W.B. Huttner, *J. Biol. Chem.*, **262**, 17026 (1987). (*Original; Chromogranin A cDNA*)
2) J. Briolat, S.D. Wu, S.K. Mahata, B. Gonthier, D. Bagnard, S. Chasserot-Golaz, K.B. Helle, D. Aunis, and M.H. Metz-Boutigue, *Cell. Mol. Life Sci.*, **62**, 377 (2005). (*Review*)
3) B.S. Sahu, P.J. Sonawane, and N.R. Mahapatra, *Cell. Mol. Life Sci.*, **67**, 861 (2010). (*Review*)
4) S.K. Mahata, M. Mahata, M.M. Fung, and D.T. O'Connor, *Regul. Pept.*, **162**, 33 (2010). (*Review*)

TIP39

Code	Compound			Price:Yen
4479-s New -20℃	**TIP39** **Tuberoinfundibular Peptide of 39 Residues (Human, Bovine)** Ser-Leu-Ala-Leu-Ala-Asp-Asp-Ala-Ala-Phe- Arg-Glu-Arg-Ala-Arg-Leu-Leu-Ala-Ala-Leu- Glu-Arg-Arg-His-Trp-Leu-Asn-Ser-Tyr-Met- His-Lys-Leu-Leu-Val-Leu-Asp-Ala-Pro (M.W. 4504.2) $C_{202}H_{325}N_{61}O_{54}S$ [277302-47-3] Purity ≧99.0% including Met(O) analog (≦1.0%) (HPLC)	Vial	0.1 mg	22,000

Ligand for Parathyroid Hormone 2 Receptor

There are two G-protein-coupled receptors for parathyroid hormone (PTH): PTH 1 receptor (PTH1R) and PTH2R. Parathyroid Hormone (Human, 1-84) [Code 4134-v] is known to exert its biological activities through PTH1R and PTH2R in human, while **TIP39 (Tuberoinfundibular Peptide of 39 Residues)** is the primary ligand for the PTH2R.

TIP39 was first isolated from the bovine hypothalamus; later the primary structure of human **TIP39** was determined to be identical to that of bovine peptide by analyzing genomic DNA[1). This particular ligand-receptor pair, TIP39-PTH2R, is localized in the brain and affords many regulatory effects on stress response, hormone release such as Arg-vasopressin, GH and prolactin, anxiety and development of fear, regulation of body temperature, and nociceptive function, among others[2-4)]. Considering this plethora of activities, **TIP39** may be useful in the study to clarify the mechanism of neuroendocrine disorders and related diseases.

1) M.R. John, M. Arai, D.A. Rubin, K.B. Jonsson, and H. Jüppner, *Endocrinology*, **143**, 1047 (2002). (*Original*)
2) L. Coutellier and T.B. Usdin, *Behav. Brain Res.*, **222**, 265 (2011). (*Pharmacol.*)
3) E.L. Dimitrov, J. Kuo, K. Kohno, and T.B. Usdin, *Proc. Natl. Acad. Sci. U.S.A.*, **110**, 13156 (2013). (*Pharmacol.*)
4) A. Dobolyi, M. Palkovits, and T.B. Usdin, *Prog. Neurobiol.*, **90**, 29 (2010). (*Review*)

Phytosulfokine

Code	Compound			Price:Yen
4477-s New -20℃	**Phytosulfokine** **PSK** **(Plant, *Asparagus officinalis* L.)** (Ammonium Form) Tyr(SO_3H)-Ile-Tyr(SO_3H)-Thr-Gln (M.W. 846.88) $C_{33}H_{46}N_6O_{16}S_2$ [179667-62-0] Purity ≧99.0% (HPLC)	Vial	0.1 mg	5,000

Potent Mitogenic Factor in Plants

O-sulfation of Tyr is an example of a posttranslational modification present in peptides and proteins, by which the modified molecule elicits the intrinsic biological function. In the animal kingdom, CCK-octapeptide (26-33) (sulfated form) [Code 4100-v], CCK-33 (human) [Code 4201-s], CCK-33 (porcine) [Code 4176-s] are well-known examples of the sulfated-Tyr-containing peptide. The same is true in higher plants: **phytosulfokine** (**PSK**) was identified in the culture medium of *Asparagus officinalis* by Matsubayashi and Sakagami in 1996[1). **PSK** is a 5-residue peptide that the Tyr residues at positions 1 and 3 are sulfated. Later, the same peptide was identified in other plants including rice and carrots; therefore **PSK** is recognized as being a widely distributed peptide in plants.

Functionally, **PSK** is considered to be a plant hormone because **PSK** stimulates: **i)** plant cell proliferation and differentiation at 3.8 nM (ED_{50}), **ii)** chlorophyll synthesis, **iii)** adventitious root and bud formation, **iv)** somatic embryogenesis, and **v)** attenuation of pattern-triggered immunity (TPI)[2-5). These activities are mediated by specific **PSK** receptor(s)[6,7).

This posttranslationally modified peptide hormone **PSK** is convincingly indispensable in research to clarify physiological functions in plants.

1) Y. Matsubayashi and Y. Sakagami, *Proc. Natl. Acad. Sci. U.S.A.*, **93**, 7623 (1996). (*Original: Structure & Pharmacol.*)
2) Y. Matsubayashi, H. Shinohara, and M. Ogawa, *Chem. Rec.*, **6**, 356 (2006). (*Review; Structure-Activiry Relationship & Receptor-Ligand Interaction*)
3) A. Bahyrycz and D. Konopińska, *J. Pept. Sci.*, **13**, 787 (2007). (*Review; Pharmacol.*)
4) D. Igarashi, K. Tsuda, and F. Katagiri, *Plant J.,* **71**, 194 (2012). (*Pharmacol.*)
5) N. Stührwohldt, R.I. Dahlke, B. Steffens, A. Johnson, and M. Sauter, *PLoS One*, **6**, e21054 (2011). (*Pharmacol.*)
6) Y. Matsubayashi, M. Ogawa, A. Morita, and Y. Sakagami, *Science*, **296**, 1470 (2002). (*Specific Receptor*)
7) Y. Matsubayashi, *J. Cell Sci.*, **116**, 3863 (2003). (*Review; Specific Receptor*)

Peptide Tool

Code	Compound			Price:Yen
3406-v	**Amyloid β-Protein (1-42, *O*-acyl isopeptide)**	Vial	0.5 mg	30,000

New

-20℃

26-*O*-acyl isoAβ1-42

(Trifluoroacetate Form)

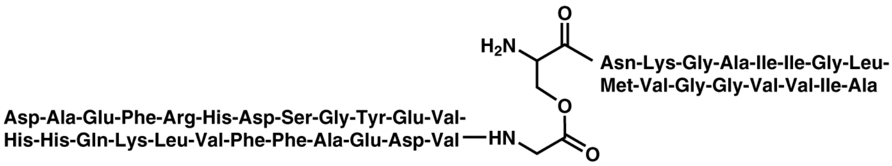
(1-25) : Asp-Ala-Glu-Phe-Arg-His-Asp-Ser-Gly-Tyr-
Glu-Val-His-His-Gln-Lys-Leu-Val-Phe-Phe-
Ala-Glu-Asp-Val-Gly

(26-42) : Ser-Asn-Lys-Gly-Ala-Ile-Ile-Gly-Leu-Met-
Val-Gly-Gly-Val-Val-Ile-Ala

(Ester bond between Gly[25] α-carboxyl group and Ser[26] β-hydroxyl group)

(M.W. 4514.0) $C_{203}H_{311}N_{55}O_{60}S$ [753459-14-2]

Purity ≧95.0% (HPLC)



pH Click Peptide for Amyloid β-Protein (Human, 1-42)

Amyloid β-protein (1-42, *O*-acyl isopeptide) is an artificial peptide designed by Professor Kiso's group[1,2]. The structural feature of this peptide is an ester linkage, instead of the native carboxamide, between Gly[25] and Ser[26], rendering this a branched peptide at Ser[26] and now feasible to dissolve in water. The ester bond from the side chain of Ser[26] is reported to be stable at pH 2.0, but easily and efficiently converted to the carboxamide bond by *O*-to-*N* acyl migration under the basic conditions such as pH 7.4. The nascent amyloid β-protein (1-42) initiates the conformational change from a random coil to a β-structure, initiating aggregation[1-3].

Our synthesis group has recently succeeded in synthesizing the **amyloid β-protein (1-42, *O*-acyl isopeptide)** by Boc chemistry using a novel isoacyl-dipeptide unit in collaboration with Professor Kiso[4]. We are very pleased to offer this as a "Peptide Tools" catalog item, giving customers further flexibility in their Alzheimer's disease research.

Amyloid β-Protein (1-42, *O*-acyl isopeptide) [Trifluoroacetate Form]	→ *O*-to-*N* Acyl Migration at pH 7.4	Amyloid β-Protein (1-42)
Structure: Random Coil at pH 2.0		Structure Change: Random Coil to β-Structure

1) Y. Sohma, M. Sasaki, Y. Hayashi, T. Kimura, and Y. Kiso, *Tetrahedron Lett.*, **45**, 5965 (2004). (*Original; Chem. Synthesis*)
2) A.Taniguchi, Y. Sohma, Y. Hirayama, H. Mukai, T. Kimura, Y. Hayashi, K. Matsuzaki, and Y. Kiso, *ChemBioChem*, **10**, 710 (2009).
3) R. Roychaudhuri, A. Lomakin, S. Bernstein, X. Zheng, M.M. Condron, G.B. Benedek, M. Bowers, and D.B. Teplow, *J. Mol. Biol.*, **426**, 2422 (2014).
4) a) T. Yoshiya, T. Uemura, T. Maruno, S. Kubo, Y. Kiso, Y. Sohma, Y. Kobayashi, K. Yoshizawa-Kumagaye, and Y. Nishiuchi, *J. Pept. Sci.*, **20**, 669 (2014); b) T. Yoshiya, T. Maruno, T. Uemura, S. Kubo, Y. Kiso, Y. Sohma, K. Yoshizawa-Kumagaye,Y. Kobayashi, and Y. Nishiuchi, *Bioorg. Med. Chem. Lett.*, **24**, 3861 (2014).

Note: We have not described the conformational characteristics of amyloid β-protein (1-42) (Code 4349-v) in our catalog. However, we actually offered all of the already shipped vials and will offer the new lot vials henceforth after confirming the conformational change in CD spectra; from a random coil to a β-structure in aqueous buffer at pH 7.4 and 37 ℃ within 24 h at the peptide concentration of 10 μM. This is also applicable to amyloid β-protein (1-43) (Code 4370-v).

Enzyme Substrate

Code	Compound			Price:Yen
3233-v New -20℃	**Nma-Phe-His-Lys(Dnp)** (Trifluoroacetate Form) [2-(Methylamino)benzoyl]-L-phenylalanyl-L-histidyl- N^{ε}-(2,4-dinitrophenyl)-L-lysine (M.W. 729.74) $C_{35}H_{39}N_9O_9$ Purity ≧98.0% (HPLC)	Vial	1 mg	10,000

Fluorescence-Quenching Substrate for Angiotensin I Converting Enzyme and Carboxypeptidase Y

1) S. Takahashi, H. Ono, T. Gotoh, K. Yoshizawa-Kumagaye, and T. Sugiyama, *Biomed. Res.*, **32**, 407 (2011).

Fmoc-Amino Acids

Code	Compound			Price:Yen
2328 New 2～10℃	**Fmoc-His(MBom)** N^{α}-9-Fluorenylmethoxycarbonyl- N^{π}-4-methoxybenzyloxymethyl-L-histidine (M.W. 527.57) $C_{30}H_{29}N_3O_6$ [1327338-56-6] Purity ≧98.0% (HPLC)	Bulk	1 g 5 g	10,000 45,000

1) H. Hibino and Y. Nishiuchi, *Tetrahedron Lett.*, **52**, 4947 (2011).
2) H. Hibino, Y. Miki, and Y. Nishiuchi, *J. Pept. Sci.*, **18**, 763 (2012).
3) K. Sakamoto, K. Sato, A. Shigenaga, K. Tsuji, S. Tsuda, H. Hibino, Y. Nishiuchi, and A. Otaka, *J. Org. Chem.*, **77**, 6948 (2012).

Code	Compound			Price:Yen
2329 New 2～10℃	**Fmoc-Cys(Dpm)** 9-Fluorenylmethoxycarbonyl-*S*-diphenylmethyl-L-cysteine (M.W. 509.62) $C_{31}H_{27}NO_4S$ [247595-29-5] Purity ≧98.0% (HPLC)	Bulk	5 g	10,000

1) M. Góngora-Benítez, L. Mendive-Tapia, I. Ramos-Tomillero, A.C. Breman, J. Tulla-Puche, and F. Albericio, *Org. Lett.*, **14**, 5472 (2012).
2) H. Hibino, Y. Miki, and Y. Nishiuchi, *J. Pept. Sci.*, **20**, 30 (2014).

Code	Compound			Price:Yen
2330 New 2～10℃	**Fmoc-Cys(Ddm)** 9-Fluorenylmethoxycarbonyl-*S*-4,4'-dimethoxydiphenylmethyl-L-cysteine (M.W. 569.67) $C_{33}H_{31}NO_6S$ [1403825-56-8] Purity ≧98.0% (HPLC)	Bulk	1 g	10,000

1) M. Góngora-Benítez, L. Mendive-Tapia, I. Ramos-Tomillero, A.C. Breman, J. Tulla-Puche, and F. Albericio, *Org. Lett.*, **14**, 5472 (2012).
2) H. Hibino, Y. Miki, and Y. Nishiuchi, *J. Pept. Sci.*, **20**, 30 (2014).

CUSTOM SERVICES ペプチド・糖のカスタム合成

1. ご希望のペプチド(Cys 含有ペプチドも含む)
   2-200 残基(200 残基を越える場合も可能です。ご相談下さい)
2. 生理活性ペプチドとその誘導体
3. 細胞膜透過性ペプチド（Tat，オリゴアルギニン，Penetratin など）
4. 各種酵素基質(MCA，AFC，*p*NA, その他の蛍光，発色基質など)
5. 消光性蛍光基質(Nma-Dnp，MOCAc-Dnp，Dabcyl-EDANS の組合せなど)
6. 酵素阻害剤(アルデヒド，フルオロメチルケトン，クロロメチルケトン，ボロン酸誘導体など)
7. ジスルフィド結合含有ペプチド(1 組，2 組，3 組以上。分子内，分子間)
8. 環状ペプチドおよび枝分かれペプチド
9. 鎖状および環状デプシペプチド
10. リン酸化ペプチド [Ser(PO_3H_2)，Thr(PO_3H_2)，Tyr(PO_3H_2)誘導体]
11. ホスホノペプチド [リン酸化ペプチドのカルバ型誘導体]
    [Ser(PO_3H_2)，Thr(PO_3H_2)，Tyr(PO_3H_2)に対応するホスファターゼ抵抗性誘導体]
12. 硫酸化ペプチド［Tyr(SO_3H)］
13. アミノ基修飾誘導体（Biotinyl 化 , Myristoyl 化 , Palmitoyl 化 , Methyl 化 , Malonyl 化 , PEG 化 , Acetyl 化 , Boc 化 , Z 化 , など種々の修飾)
14. チオール基修飾誘導体（Farnesyl 化，Geranyl 化，Biotinyl 化など）
15. 蛍光標識ペプチド(FITC, Rhodamine, BODIPY, DY- シリーズなど 380 nm-730 nm に対応)
16. 糖ペプチド [Asn(GlcNAc), Ser/Thr(GalNAc), Ser/Thr(Gal-GalNAc), Ser/Thr(Neu-Gal-GalNAc), Ser/Thr(GlcNAc), 1-Deoxyfructosyl 含有ペプチドなど]
17. 非天然アミノ酸含有ペプチド（ハイプシン , システインスルフィン酸　他多数）
18. ペプチド結合の修飾(還元型、スタチン型など)
19. アミノ酸誘導体 , 保護ペプチド
20. 安定同位体ラベルアミノ酸含有ペプチド(^{13}C，^{15}N，^{2}H など)
21. ペプチドアルコール
22. 糖関連化合物（ガングリオシド , Lipid A, 糖ヌクレオチドなど）
23. 一般有機化合物
24. その他

受託合成量：標準 10mg ～ 25mg から g、kg オーダーまで承ります。(お見積り依頼の際に、ご相談下さい)

納　　期：固相法にて合成可能な通常のペプチド 25mg の場合：通常 2-4 週間
液相法などその他の方法で合成する場合はご相談させていただきます。

保 証 純 度：通常、トリフルオロ酢酸塩でご提供いたします。他の塩をご希望の場合はご相談下さい。
規格　(1）逆相 HPLC で検定：90%以上（精製品）
(2）逆相 HPLC で検定：95% 以上（精製品）
(3）逆相 HPLC で検定：99% 以上（精製品）
通常、HPLC チャート、アミノ酸分析結果、質量分析結果を添付いたします。
その他の分析項目につきましてはご相談させていただきます。

価　　格：個別にお見積りいたしますので、弊社 Web Site から、あるいは E-mail、Fax にてご相談下さい。

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GMP 対応、治験薬 GMP 対応など個別にご相談させていただきます。

ペプチド合成依頼書

（□見積依頼書　□発注）

年　　月　　日

ご依頼者

ご 住 所：〒□□□-□□□□

勤 務 先：　　　　　　　　　　　　　　　　ご所属：

フリガナ
お 名 前：

T E L：　　-　　-　　　　（内線）

F A X：　　-　　-

E-mail：

アミノ酸配列

（アミノ酸配列は1文字表記、3文字表記どちらでも結構です）

N末端　　　　　　　　　　　　　　　　　　　　　　　　　　　　C末端→

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20

ペプチド量：　□ 25 mg（標準量）　□ 50 mg　□　　mg　□　　g　□　　kg

純　度（逆相HPLC）：□ 90%以上保証（精製品）　□ 95%以上保証（精製品）

ご用途：　□ 抗原（抗体作製）用　□ その他（　　　　）

コンジュゲーション・抗体作製　　お差し仕えなければご記入下さい。

コンジュゲーション：□ 希望する　□ 希望しない

希望結合部位：□ N端　□ C端　□ その他（　　　）

キャリアー蛋白質の種類：□ BSA　□ KLH　□ OVA　□ その他（　　　）

抗体作製（ウサギ）：□ 希望する（　羽）　□ 希望しない

抗体アフィニティー精製：□ 希望する　□ 希望しない

担体への結合：□ ペプチド　□ その他（　　　）

抗体の標識：□ ビオチン標識　□ パーオキシダーゼ標識（過ヨウ素酸法）

備考（ご要望事項など）

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