Product Data Sheet

Product Name: APETx2 TFA
Cat. No.: GC65272

Chemical Properties

Cas. No.			
Formula	C198H281F3N54O62S6	M.Wt	4675.02
Solubility	Saline : 0.5 mg/mL (0.11 mM; Need ultrasonic and warming)	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure	APETx2 TFA		

Protocol

Cell experiment [1]:

Cell lines	Articular chondrocytes
Preparation Method	Articular chondrocytes were cultured in DMEM supplemented with 10% fetal bovine serum (FBS) at 37°C, 5% CO_2. Cells were pretreated with ASIC3-specific blocker APETx2 (3μM) for 1 hour, and exposure to pH 6.0 solution for 3 hours.
Reaction Conditions	3μM; 1-hour pretreatment.

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Applications	Pretreatment with APETx2, in combination with the ASIC1a-specific blocker PcTx1, significantly attenuated acidosis (pH=6.0)-induced chondrocyte cytotoxicity and apoptosis. This protective effect was characterized by increased cell viability, reduced LDH release, decreased intracellular Ca^{2+} concentration ($[Ca^{2+}]i$) elevation, reduced apoptotic rate, and inhibition of the p38 and ERK1/2 MAPK signaling pathways. Additionally, the combination treatment (PcTx1 and APETx2) reversed the acid-induced decrease in type II collagen levels.

Animal experiment [2]:

Animal models	Male Sprague-Dawley rats (with MIA-induced osteoarthritis model)
Preparation Method	A single dose of monosodium iodoacetate (MIA, 3mg dissolved in 50μl saline) was injected into the left knee joint to induce osteoarthritis. Rats were treated with intra-articular injections of the selective ASIC3 blocker APETx2 (2.5μg/kg) daily, either during the early phase (Days 1-7 after MIA) or the late phase (Days 7-13 after MIA). Pain-related behaviors (weight distribution asymmetry and mechanical hyperalgesia) were assessed at specified time points, and histological evaluation of knee joints was performed at Day 14.
Dosage form	2.5μg/kg; intra-articular injection; Daily continuous injection.

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Applications	Continuous administration of APETx2 inhibited the upregulation of ASIC3 in knee joint afferent neurons. APETx2 significantly reduced mechanical hyperalgesia (secondary hyperalgesia) in both early- and late-phase treatment groups. APETx2 also significantly inhibited weight distribution asymmetry in the early-phase group at Day 3. Furthermore, early administration of APETx2 (Days 1-7) prevented cartilage damage and reduced the severity of osteoarthritis, as evidenced by improved histological scores (modified Mankin score).

References:

[1] Zhou RP, Ni WL, Dai BB, et al. ASIC2a overexpression enhances the protective effect of PcTx1 and APETx2 against acidosis-induced articular chondrocyte apoptosis and cytotoxicity. Gene. 2018 Feb 5;642:230-240.
[2] Izumi M, Ikeuchi M, Ji Q, et al. Local ASIC3 modulates pain and disease progression in a rat model of osteoarthritis. J Biomed Sci. 2012 Aug 21;19(1):77.

Background

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APETx2 is a peptide toxin derived from *Anthopleura elegantissimaand* serves as a selective, reversible inhibitor of the acid-sensing ion channel 3 (ASIC3)[1-2]. By inhibiting the activity of the ASIC3 channel, APETx2 blocks acid-induced pain signaling. APETx2 can be used in research related to inflammatory pain, post-infectious irritable bowel syndrome, and gastric mucosal injury[3-4].

In vitro, rat articular chondrocytes were pretreated with APETx2 (3μM) and PcTx1 (100ng/ml) for 1 hour, followed by incubation under acidic conditions (pH=6.0) for 3 hours. APETx2 significantly alleviated acidosis-induced cytotoxicity and apoptosis, exerting a chondroprotective effect by reducing intracellular Ca^{2+} levels and inhibiting the phosphorylation of the p38/ERK1/2 MAPK signaling pathway[5]. Under magnesium-free medium conditions (used to induce epileptiform discharge), primary hippocampal neurons were incubated with APETx2 (63nM) for 1 hour. APETx2 significantly increased the frequency of burst discharges induced by the magnesium-free medium[6].

In vivo, APETx2 (20pmol per mouse) was injected into the Zusanli acupoint (ST36) of a fibromyalgia mouse model. By antagonizing ASIC3, APETx2 significantly reduced mechanical hyperalgesia on day 14 post-induction and decreased the overexpression of pain-related channel proteins ASIC3, Nav1.7, and Nav1.8 in the dorsal root ganglia, spinal cord, and thalamus[7]. In a rat model of osteoarthritis, daily continuous intra-articular injections of APETx2 (2.5μg/kg) for 7 days, APETx2 significantly inhibited weight-bearing asymmetry and secondary mechanical hyperalgesia in the knee joint. APETx2 also effectively prevented articular cartilage damage by reducing chondrocyte loss and matrix destruction[8].

References:
[1] Yuan L, Xiao H, Li H, et al. APETx2 regulates intestinal motility and visceral sensitivity in post-infectious irritable bowel syndrome mice through 5-HT signalling pathway. J Pharm Pharmacol. 2023 Apr 17;75(5):712-717.
[2] Li J, Wei Y, Wang Y, et al. Metabolomics study of APETx2 post-conditioning on myocardial ischemia-reperfusion injury. Front Pharmacol. 2024 Dec 6;15:1470142.
[3] Diochot S, Baron A, Rash LD, et al. A new sea anemone peptide, APETx2, inhibits ASIC3, a major acid-sensitive channel in sensory neurons. EMBO J. 2004 Apr 7;23(7):1516-25.

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[4] Chagot B, Escoubas P, Diochot S, et al. Solution structure of APETx2, a specific peptide inhibitor of ASIC3 proton-gated channels. Protein Sci. 2005 Aug;14(8):2003-10.
[5] Zhou RP, Ni WL, Dai BB, et al. ASIC2a overexpression enhances the protective effect of PcTx1 and APETx2 against acidosis-induced articular chondrocyte apoptosis and cytotoxicity. Gene. 2018 Feb 5;642:230-240.
[6] Cao Q, Xiao ZM, Wang X, et al. Inhibition of Acid Sensing Ion Channel 3 Aggravates Seizures by Regulating NMDAR Function. Neurochem Res. 2018 Jun;43(6):1227-1241.
[7] Yen LT, Hsieh CL, Hsu HC, et al. Preventing the induction of acid saline-induced fibromyalgia pain in mice by electroacupuncture or APETx2 injection. Acupunct Med. 2020 Jun;38(3):188-193.
[8] Izumi M, Ikeuchi M, Ji Q, et al. Local ASIC3 modulates pain and disease progression in a rat model of osteoarthritis. J Biomed Sci. 2012 Aug 21;19(1):77.

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