

## Product Data Sheet

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Product Name: GsMTx4

Cat. No.: GC38465

### Chemical Properties

Cas. No. 1209500-46-8

Chemical Name Gly-Cys-Leu-Glu-Phe-Trp-Trp-Lys-Cys-Asn-Pro-Asn-Asp-Asp-Lys-Cys-Cys-Arg-Pro-Lys-Leu-Lys-Cys-Ser-Lys-Leu-Phe-Lys-Leu-Cys-Asn-Phe-Ser-Phe

Formula  $C_{185}H_{279}N_{49}O_{45}S_6$  M.Wt 4101.89

Solubility Water : 16.67 mg/mL Storage -20°C, Sealed storage, away from moisture and light.

General tips For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C 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

GCLEFWWWKCNPNDDKCCRPKLKCSKLFKLCNFSF-NH<sub>2</sub>

### Protocol

#### Cell experiment [1]:

Cell lines HEK 293 cells

**Caution: Product has not been fully validated for medical applications. For research use only.**

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For Piezo1 channels, the extracellular solution contained 145 mM NaCl, 5 mM KCl, 3 mM MgCl<sub>2</sub>, 0.1 mM CaCl<sub>2</sub>, and 10 mM HEPES (pH 7.4). The pipette Preparation method solution contained 133 mM CsCl, 10 mM HEPES (pH 7.4). The inhibition produced by application of GsMTx4 was followed by ~60 s of washout, followed by application of WT GsMTx4 as a control.

Reaction Conditions 5  $\mu$ M GsMTx4, 40s

**Applications**

GsMTx4 is a spider venom peptide that inhibits cationic mechanosensitive channels (MSCs). A model placing GsMTx4 at the membrane surface, where it is stabilized by the lysines, and occupying a small fraction of the surface area in unstressed membranes. When applied tension reduces lateral pressure in the lipids, the peptides penetrate deeper acting as “area reservoirs” leading to partial relaxation of the outer monolayer, thereby reducing the effective magnitude of stimulus acting on the MSC gate.

### Animal experiment [2]:

**Animal models** Male C57BL/6 mice

**Dosage form**

To the WT and Clock $\Delta$ 19/ $\Delta$ 19 mice, GsMTx4 or vehicle was administered via intraperitoneal injection (IP) at two different time-points, Z12- and ZT0-IP (higher and lower Piezo1 expression periods in the WT mice, respectively). The WT and Clock $\Delta$ 19/ $\Delta$ 19 mice were injected with 0.75 (low dose-IP) or 1.5 mg/kg (high dose-IP) of GsMTx4 in 100  $\mu$ L of distilled water.

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### Applications

VF decreased at ZT12-IP in WT mice only with high dose of GsMTx4 but showed no effects in Clock $\Delta$ 19/ $\Delta$ 19 mice. GsMTx4 did not affect Uvol in both mice at ZT12-IP. A decrease in Uvol was observed in both mice at ZT0-IP; however, it was unrelated to GsMTx4-IP. The effects of GsMTx4 changed associated with the circadian clock and Piezo1 expression level.

### References:

- [1]. Gnanasambandam R, et al. GsMTx4: Mechanism of Inhibiting Mechanosensitive Ion Channels. *Biophys J*. 2017 Jan 10;112(1):31-45.
- [2]. Ihara, Tatsuya, et al. "Different effects of GsMTx4 on nocturia associated with the circadian clock and Piezo1 expression in mice." *Life Sciences* 278 (2021): 119555.

### Background

GsMTx4 is a 34 amino acid spider venom peptide and belongs to the huwentoxin-1 family[1]. GsMTx4 selectively inhibits cation-permeable mechanosensitive channels (MSCs) belonging to the Piezo, TRPC1 and TRPC6 channels.

GsMTx4 is similar to many other channel-active peptides isolated from spider venom, which are small (3–5 kD) amphipathic molecules built on a conserved inhibitory cysteine-knot (ICK) backbone[4]. GsMTx4 has high potency for inhibiting mechanosensitive channels, and its inhibition is not stereospecific, i.e., both its enantiomers (L- and D-form) inhibiting MSCs[3].

GsMTx4 significantly attenuates bladder hyperactivity[2]. Intraperitoneal injection of GsMTx-4 has been shown to reduce mechanical hyperalgesia induced by carrageenan or sciatic nerve injury[5], although it does not inhibit SAC currents in cultured DRG neurons[6].

GsMTx4 is an important pharmacological tool for identifying the role of these excitatory MSCs in normal physiology and pathology[4].

### References:

- [1]. Suchyna TM, et al. Identification of a peptide toxin from *Grammostola spatulata* spider venom

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- [2]. Liu Q, et al. Increased Piezo1 channel activity in interstitial Cajal-like cells induces bladder hyperactivity by functionally interacting with NCX1 in rats with cyclophosphamide-induced cystitis. Exp Mol Med. 2018 May 7;50(5):60.
- [3]. Suchyna T.M., Tape S.E., Gottlieb P.A. Bilayer-dependent inhibition of mechanosensitive channels by neuroactive peptide enantiomers. Nature. 2004;430:235–240.
- [4]. Gnanasambandam R, et al. GsMTx4: Mechanism of Inhibiting Mechanosensitive Ion Channels. Biophys J. 2017 Jan 10;112(1):31-45.
- [5]. Park SP, et al. A tarantula spider toxin, GsMTx4, reduces mechanical and neuropathic pain. Pain. 2008;137:208–217.
- [6]. Drew LJ, , et al.. High-threshold mechanosensitive ion channels blocked by a novel conopeptide mediate pressure-evoked pain. PLoS ONE. 2007;2:e515.

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