
Product Data Sheet

Product Name: MOTS-c
Cat. No.: GC25648

Chemical Properties

Cas. No. 1627580-64-6

Formula $C_{101}H_{152}N_{28}O_{22}S_2$ M.Wt 2174.6

Solubility Storage Store at -20°C

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

Protocol**Cell experiment [1]:**

Cell lines HEK293 cells

Preparation Method HEK293 cells are usually cultured in the Dulbecco-modified Eagle's Medium (DMEM). Since the main function of mitochondria involves metabolic processes, the next step is to investigate the impact of MOTS-c on cell metabolism using an unbiased global metabolomics analysis method in vitro. Using a "function-enhancing" model, studies were conducted using HEK293 cells with stable overexpression of MOTS-c (MOTS-c-ST) or with 10µM synthetic MOTS-c for 24 hours and 72 hours of exogenous treatment. Microarray analysis was performed on HEK293 cells treated with MOTS-c for 4 hours and 72 hours. The level of AICAR measured in MOTS-c-ST cells by mass spectrometry.

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

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Reaction Conditions 10 μ M; 4h, 72h

Applications MOTS-c targets the methionine-folate cycle, increases the level of AICAR, and activates AMPK.

**Animal experiment
[1]:**

Animal models ICR mice

Preparation Method In all in vivo experiments, MOTS-c was injected intraperitoneally daily. Eight-week-old CD-1 (ICR) mice were purchased from Harlan Company. C57BL/6 mice were purchased from Jackson Laboratory. The mice were fed a high-fat diet (containing 60% calories) and a matched control diet for 8 weeks. The diet was changed twice a week, and body weight and food intake were recorded daily (N=10). Seven days after intraperitoneal injection of MOTS-c, a glucose tolerance test (GTT) was conducted. Subsequently, a hyperinsulinemic-euglycemic clamp test was performed to quantify the effect of 7 days of MOTS-c treatment on systemic insulin sensitivity.

Dosage form 5mg/kg/day for 7 days; i.p.

Applications MOTS-c significantly enhanced the glucose clearance rate stimulated by insulin and improved insulin sensitivity in skeletal muscle.

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References:

[1] Lee C, Zeng J, Drew BG, Sallam T, Martin-Montalvo A, Wan J, Kim SJ, Mehta H, Hevener AL, de Cabo R, Cohen P. The mitochondrial-derived peptide MOTS-c promotes metabolic homeostasis and reduces obesity and insulin resistance. *Cell Metab.* 2015 Mar 3;21(3):443-54.

Background

MOTS-c is a mitochondrial-derived polypeptide with metabolic regulatory functions^[1]. MOTS-c exerts anti-injury and anti-inflammatory effects by activating the AMPK pathway and inhibiting the MAP kinase-c-fos signaling pathway^[2]. MOTS-c can be used in studies on stress, inflammation, metabolism, neuroprotection, and aging^[3].

In vitro, MOTS-c (0-100 μ M; 8-24 hours) can promote the phosphorylation of AMPK (Thr 172) and Akt (Ser 473) in HEK 293 cells in a time- and dose-dependent manner^[4]. Different concentrations of MOTS-c (0, 2.5, 5, 10, 20 and 40 μ M; 24 hours) would weaken the inhibitory effect of hypoxia treatment on the inhibition of DR4, DR5, FADD and caspase-8 in HCC cells. MOTS-c weakens the resistance of liver cancer cells to TRAIL-induced apoptosis by activating MEF2A^[5].

In vivo, male C57 BL/6 mice treated with MOTS-c (5mg/kg/day; i.p.) for 7 days significantly enhanced insulin-stimulated glucose clearance rate and improved insulin sensitivity in skeletal muscle^[4]. Treating mice with MOTS-c (50mg/kg; i.p.) 4 hours before formalin treatment significantly reduced the levels of pro-inflammatory cytokines in mouse serum and increased the levels of anti-inflammatory cytokines. Additionally,

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MOTS-c treatment significantly increased the phosphorylation level of AMPK α , inhibited the activation of spinal extracellular signal-regulated kinase (ERK), c-Jun amino-terminal kinase (JNK), and P38 in mice induced by formalin, as well as the expression of c-fos [6].

References:

- [1] Benayoun B A, Lee C. MOTS-c: a mitochondrial-encoded regulator of the nucleus[J]. *Bioessays*, 2019, 41(9): 1900046.
- [2] Yin X, Jing Y, Chen Q, Abbas AB, Hu J, Xu H. The intraperitoneal administration of MOTS-c produces antinociceptive and anti-inflammatory effects through the activation of AMPK pathway in the mouse formalin test. *Eur J Pharmacol*. 2020 Mar 5;870:172909.
- [3] Wan W, Zhang L, Lin Y, et al. Mitochondria-derived peptide MOTS-c: effects and mechanisms related to stress, metabolism and aging[J]. *Journal of Translational Medicine*, 2023, 21(1): 36.
- [4] Lee C, Zeng J, Drew BG, Sallam T, Martin-Montalvo A, Wan J, Kim SJ, Mehta H, Hevener AL, de Cabo R, Cohen P. The mitochondrial-derived peptide MOTS-c promotes metabolic homeostasis and reduces obesity and insulin resistance. *Cell Metab*. 2015 Mar 3;21(3):443-54.
- [5] Shen H, Nie J, Wang X, et al. MOTS-c relieves hepatocellular carcinoma resistance to TRAIL-induced apoptosis under hypoxic conditions by activating MEF2A[J]. *Experimental Cell Research*, 2025, 444(1): 114354.
- [6] Yin X, Jing Y, Chen Q, et al. The intraperitoneal administration of MOTS-c produces antinociceptive and anti-inflammatory effects through the activation of AMPK pathway in the mouse formalin test[J]. *European journal of pharmacology*, 2020, 870: 172909.

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