

Product Data Sheet

Product Name: Nangibotide TFA

Cat. No.: GC63949

Chemical Properties

Cas. No. 2014384-91-7

Formula C₅₆H₈₃F₃N₁₄O₂₄S₂ M.Wt 1457.46

Solubility DMSO : 50 mg/mL (34.31 mM; Need ultrasonic) Storage Store at -20°C, protect from light, stored under nitrogen

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

LQEEDAGEYGCM-NH₂ (TFA salt)

Protocol

Cell experiment [1]:

Cell lines MC3T3-E1 mouse osteoblast cell line

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MC3T3-E1 mouse osteoblast cell line was used for this study. MC3T3-E1 cells were grown in α -MEM containing 10% FBS and 1% penicillin/streptomycin in a cell incubator under 5% CO₂ at 37°C. Cell Counting Kit-8 (CCK-8) test was used to measure cell viability and proliferation. The cells were grown at a density of 6×10^3 cells/well in 96-well plates for 12h for adhesion. To determine the toxicity of Nangibotide TFA, the cells were treated with Nangibotide TFA at concentrations of 0, 25, 50, 100, and 200 μ g/mL for 1, 3, or 5 days. To determine whether Nangibotide TFA could restore the proliferation of MC3T3-E1 cells, 10ng/mL TNF- α was added to various concentrations of Nangibotide TFA. In addition, 10 μ L of CCK-8 per well was then added to the cells. After incubating at 37°C for 2h, the cells were assessed by spectrophotometry.

Reaction Conditions 0, 25, 50, 100, and 200 μ g/mL for 1, 3, or 5 days

Applications Nangibotide TFA significantly enhanced osteoblast proliferation.

Animal experiment [2]:

Animal models C57BL/6 J mice

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For the acute lung injury (ALI) model, C57BL/6 J mice were randomly grouped and treated with lipopolysaccharide (LPS) (5mg/kg) intratracheal injection (*i.t.*) for 6h. Control animals received saline respectively. For survival study, mice were treated with a lethal dose of LPS (20mg/kg, *i.t.*). Survival rate was monitored every 12h for 3 days after LPS injection. Mice were received saline, antagonistic TREM-1 peptide Nangibotide TFA (5mg/kg) or sequence-scrambled control peptide LRS (5mg/kg) respectively via intravenous injection (*i.v.*) 2h before LPS administration. Lung tissue samples were collected for further analysis.

Dosage form 5mg/kg; *i.v.* ; 2h before LPS administration

Applications Nangibotide TFA attenuated LPS-induced acute lung injury in mice by reducing pulmonary inflammation (decreasing MPO activity), lowering the lung wet/dry weight ratio, and inhibiting NLRP3 inflammasome activation (reducing NLRP3 protein expression).

References:

- [1] Zhong Y, Xu Y, Xue S, et al. Nangibotide attenuates osteoarthritis by inhibiting osteoblast apoptosis and TGF- β activity in subchondral bone. *Inflammopharmacology*. 2022;30(3):1107-1117.
- [2] Liu T, Zhou Y, Li P, et al. Blocking triggering receptor expressed on myeloid cells-1 attenuates lipopolysaccharide-induced acute lung injury via inhibiting NLRP3 inflammasome activation. *Sci Rep*. 2016;6:39473.

Background

Nangibotide TFA is a synthetic peptide and TREM-1 receptor inhibitor^[1]. TREM-1 (Triggering Receptor Expressed on Myeloid Cells-1) is an immune receptor belonging to the immunoglobulin superfamily, primarily expressed on the surface of myeloid cells such as monocytes, macrophages, and neutrophils^[2]. This receptor plays a crucial role in amplifying inflammatory responses,

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significantly enhancing the host's inflammatory response to pathogens^[3]. By targeting TREM-1, Nangibotide TFA can be used in research for conditions such as septic shock, osteoarthritis, acute lung injury, and acute liver failure^[4-7].

In vitro, treatment of MC3T3-E1 cells with Nangibotide TFA (50 or 100µg/mL; 7-21 days) significantly reversed the inhibition of osteogenic differentiation, increased alkaline phosphatase activity, calcium nodule formation, and the expression of Runx2, Osterix, and COL1A1 protein^[5].

In vivo, Nangibotide TFA (5mg/kg; i.p.; every 2 days for 4 weeks) significantly alleviated cartilage degeneration, improved subchondral bone microstructure, and inhibited osteoblast apoptosis in ACLT-induced osteoarthritic mice^[5]. Nangibotide TFA (5mg/kg; i.v.; administered 2 hours before LPS injection) attenuated LPS-induced acute lung injury in mice by reducing pulmonary inflammation (decreasing MPO activity), lowering the lung wet/dry weight ratio, and inhibiting NLRP3 inflammasome activation (reducing NLRP3 protein expression)^[6]. Nangibotide TFA (5mg/kg; i.v.; administered 1 hour after TAA injection) promoted liver repair in thioacetamide-induced acute liver failure mice by improving inflammation resolution and liver regeneration^[7].

References:

- [1] Cuvier V, Lorch U, Witte S, et al. A first-in-man safety and pharmacokinetics study of nangibotide, a new modulator of innate immune response through TREM-1 receptor inhibition. *Br J Clin Pharmacol*. 2018;84(10):2270-2279.
- [2] Bouchon A, Dietrich J, Colonna M. Cutting edge: inflammatory responses can be triggered by TREM-1, a novel receptor expressed on neutrophils and monocytes. *J Immunol*. 2000;164(10):4991-4995.
- [3] Bouchon A, Facchetti F, Weigand MA, Colonna M. TREM-1 amplifies inflammation and is a crucial mediator of septic shock. *Nature*. 2001;410(6832):1103-1107.
- [4] François B, Wittebole X, Ferrer R, et al. Nangibotide in patients with septic shock: a Phase 2a randomized controlled clinical trial. *Intensive Care Med*. 2020;46(7):1425-1437.
- [5] Zhong Y, Xu Y, Xue S, et al. Nangibotide attenuates osteoarthritis by inhibiting osteoblast apoptosis and TGF-β activity in subchondral bone. *Inflammopharmacology*. 2022;30(3):1107-1117.
- [6] Liu T, Zhou Y, Li P, et al. Blocking triggering receptor expressed on myeloid cells-1 attenuates lipopolysaccharide-induced acute lung injury via inhibiting NLRP3 inflammasome activation. *Sci Rep*. 2016;6:39473.
- [7] Wang Y, Xie X, Liu H, Liu H, Jiang H. LR12 Promotes Liver Repair by Improving the Resolution of

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Inflammation and Liver Regeneration in Mice with Thioacetamide- (TAA-) Induced Acute Liver Failure. Mediators Inflamm. 2021;2021:2327721.

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