

Product Data Sheet

Product Name: GO-203 TFA

Cat. No.: GC64914

Chemical Properties

Cas. No. 1222186-26-6

Formula $C_{89}H_{171}F_3N_{52}O_{21}S_2$ M.Wt 2426.77

Solubility Water : 50 mg/mL (20.60 mM; Need ultrasonic) Storage -20°C, away from moisture

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

RRRRRRRRRCQCRRKN (TFA salt)

Protocol

Cell experiment [1]:

Cell lines COLO-205 colorectal cancer cells

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Preparation Method Human COLO-205 colon cancer cells were cultured in RPMI containing 10% heat-inactivated fetal bovine serum 100µg/ml streptomycin, 100U/ml penicillin and 2mmol/L-glutamine. Authenticity of the cells was confirmed by short tandem repeat (STR) analysis. Mycoplasma contamination testing was done using kit. The cells were treated with GO-203 TFA (5µM) or control peptide CP-2 for 3 days. Then cells were collected for further analyses.

Reaction Conditions 5µM; 3 days

Applications Treatment of COLO-205 colorectal cancer cells with GO-203 TFA reduced TIGAR protein, lowered GSH, doubled intracellular ROS, and collapsed mitochondrial membrane potential.

Animal experiment [2]:

Animal models Female C57BL/6J mice

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Preparation Method	Female C57BL/6J mice (6-8 weeks old) were maintained in a specific pathogen-free facility with free access to standard fodder and water and kept in a controlled environment (22°C±2°C, 55%±5% humidity) under a 12-h light/dark cycle. Mice were divided into four groups (n=6/group): control, OVA/LPS and OVA/LPS+GO-203 TFA. Mice in the OVA/LPS, OVA/LPS+GO-203 TFA groups were sensitized by intraperitoneally injecting 100µg of sensitized grade V OVA and 1mg of aluminum hydroxide on days 0, 7, and 14. Subsequently, the sensitized animals were intranasally administered with 75µg of OVA and 3.5µg of LPS on days 21, 22, and 23. Mice in the control group were intraperitoneally injected and intranasally administered with an equal volume of phosphate-buffered saline (PBS) on the corresponding days. Mice in the OVA/LPS+GO-203 TFA group were intraperitoneally injected with the MUC1 inhibitor GO-203 TFA (20mg/kg) 2h before each challenge. The mice in the other groups were intraperitoneally injected with the same volume and concentration of DMSO solvent. All mice were anesthetized, and bronchoalveolar lavage fluid (BALF) and lung tissue were collected for subsequent experiments on day 24.
Dosage form	20mg/kg; i.p; 2h before each challenge on days 21, 22, 23
Applications	GO-203 TFA amplified TLR4/MyD88/NF-κB signaling, heightened NLRP3 inflammasome-mediated pyroptosis and doubled airway neutrophil counts in OVA/LPS-induced asthmatic mice.

References:

- [1] Ahmad R, Alam M, Hasegawa M, et al. Targeting MUC1-C inhibits the AKT-S6K1-eIF4A pathway regulating TIGAR translation in colorectal cancer. *Mol Cancer*. 2017;16(1):33.
- [2] Liu L, Zhou L, Wang L, et al. MUC1 attenuates neutrophilic airway inflammation in asthma by reducing NLRP3 inflammasome-mediated pyroptosis through the inhibition of the TLR4/MyD88/NF-κB pathway. *Respir Res*. 2023;24(1):255.

Background

GO-203 TFA is a potent MUC1-C oncoprotein inhibitor^[1]. MUC1-C is an oncogenic transmembrane

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subunit that drives tumor survival, stemness and drug resistance by constitutively activating inflammatory and PI3K-AKT signaling pathways^[2]. GO-203 TFA is an all D-amino acid peptide that consists of a poly-R transduction domain linked to a CQCRRKN motif that binds to the MUC1-C cytoplasmic tail and blocks MUC1-C homodimerization^[3]. GO-203 TFA is usually used to elucidate targeted-therapy mechanisms in colorectal and other malignancies^[4].

In vitro, combined treatment of U266 and RPMI8226 multiple-myeloma cells with GO-203 TFA (2.5µM; 72h) plus bortezomib synergistically lowers glutathione (GSH), raises ROS, down-regulates TP53-inducible glycolysis and apoptosis regulator (TIGAR), and drives PI/annexin-V-positive cell death^[5]. Treatment of MUC1-positive SKCO-1 and COLO-205 colorectal cancer cells with GO-203 TFA (5µM; 3 days) reduced TIGAR protein, lowered GSH, doubled intracellular ROS, and collapsed mitochondrial membrane potential^[6].

In vivo, GO-203 TFA (20mg/kg; i.p; 2h before each challenge on days 21, 22, 23) amplified TLR4/MyD88/NF-κB signaling, heightened NLRP3 inflammasome-mediated pyroptosis and doubled airway neutrophil counts in ovalbumin (OVA)/lipopolysaccharide (LPS)-induced asthmatic mice^[7].

References:

- [1] Hasegawa M, Sinha RK, Kumar M, et al. Intracellular Targeting of the Oncogenic MUC1-C Protein with a Novel GO-203 Nanoparticle Formulation. *Clin Cancer Res.* 2015;21(10):2338-2347.
- [2] Yasumizu Y, Rajabi H, Jin C, et al. MUC1-C regulates lineage plasticity driving progression to neuroendocrine prostate cancer. *Nat Commun.* 2020;11(1):338.
- [3] Kharbanda A, Rajabi H, Jin C, et al. Targeting the oncogenic MUC1-C protein inhibits mutant EGFR-mediated signaling and survival in non-small cell lung cancer cells. *Clin Cancer Res.* 2014;20(21):5423-5434.
- [4] Shiba S, Miki A, Ohzawa H, et al. Functional Expression of Mucin1 in Human Duodenal Adenocarcinoma. *J Surg Res.* 2019;238:79-89.
- [5] Yin L, Kufe T, Avigan D, Kufe D. Targeting MUC1-C is synergistic with bortezomib in downregulating TIGAR and inducing ROS-mediated myeloma cell death. *Blood.* 2014;123(19):2997-3006.
- [6] Ahmad R, Alam M, Hasegawa M, et al. Targeting MUC1-C inhibits the AKT-S6K1-eIF4A pathway regulating TIGAR translation in colorectal cancer. *Mol Cancer.* 2017;16(1):33.
- [7] Liu L, Zhou L, Wang L, et al. MUC1 attenuates neutrophilic airway inflammation in asthma by

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reducing NLRP3 inflammasome-mediated pyroptosis through the inhibition of the TLR4/MyD88/NF- κ B pathway. *Respir Res.* 2023;24(1):255.

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