Product Data Sheet

Product Name: FSLLRY-NH2
Cat. No.: GC10790

Chemical Properties

Cas. No.	245329-02-6		
SMILES	CC(C[C@@](/N=C(O)/[C@](/N=C(O)/[C@](/N=C(O)/[C@](N)([H])CC1=CC=CC=C1)([H])CO)([H])CC(C)C)([H])/C(O)=N/[C@@](/C(O)=N/[C@@](C(O)=N)([H])CC2=CC=C(O)C=C2)([H])CCCNC(N)=N)C		
Formula	$C_{39}H_{60}N_{10}O_8$	M.Wt	796.97
Solubility	≥ 26.9mg/mL in DMSO	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	FSLLRY-NH2		

Protocol

Cell experiment [1]:

Cell lines	HepG2 cells

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Preparation Method	HepG2 cells grown in a six-well plate were stimulated with hydrogen peroxide (100, 200, 300, 400, 600μM) and FSLLRY-NH2 (100, 150, 200, 250, 300μM) for 24h and cell lysates prepared. Equal amounts of protein from each lysate were then separated by electrophoresis on SDS polyacrylamide gels (10–14%). Proteins were then transferred to an NC membrane using a Power Pac 1000 power supply. To block any nonspecific binding, the nitrocellulose (NC) membrane was incubated in 5% nonfat dry milk, or in TBST, for greater than 60min, followed by four rinses in milk-free TBST. The membranes were incubated overnight at 4℃ with shaking with primary antibodies raised against PAR2, IL 1b, IL-8, TNF-a, and SAPK/JNK, followed by four washes with TBS containing 0.1% Tween 20. This was followed by 90min incubation in horseradish peroxidase-conjugated secondary antibody. Immuno-reactive proteins were detected using the ECL reagent. Molecular masses were estimated by comparison with a pre-stained molecular mass marker. To confirm the uniformity of protein loading, the same blots were subsequently stripped with western blot stripping buffer and re-probed with an anti-actin antibody. The results were analyzed using Quantity One analysis software. The percent of PAR2 expression or IL-1b, IL-8, TNF-a, SAPK/JNK expression were calculated against control bands.
Reaction Conditions	100-300μM; 24h
Applications	FSLLRY-NH2 reduces the level of the pro-inflammatory genes IL-8, IL-1b, and TNF-α induced by H_2O_2, through the SAPK/JNK pathways in HepG2 cells.

Animal experiment [2]:

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Animal models	Asphyxial cardiac arrest (ACA)-induced rat model
Preparation Method	One hour after ACA, FSLLRY-NH2 was diluted in 20% ethanol and administered intranasally. Briefly, the animals were placed in supine position under 2% isoflurane anesthesia. A total volume of 30 microliters (μL) of vehicle (20% ethanol) or FSLLRY-NH2 (50μg/rat) in 20% ethanol was administered to the left and right nares, alternately administering 5μL in one naris every 2 minutes for a period of 10 minutes.
Dosage form	50μg; nas; single administration
Applications	FSLLRY-NH2 treatment significantly improved neurological outcomes and reduced the number of degenerating hippocampal neurons after ACA.

References:

[1]. Lee Y J, Kim S J, Kwon K W, et al. Inhibitory effect of FSLLRY-NH2 on inflammatory responses induced by hydrogen peroxide in HepG2 cells[J]. Archives of

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[2]. Ocak U, Ocak P E, Huang L, et al. FSLLRY-NH2 improves neurological outcome after cardiac arrest in rats[J]. Turk Neurosurg, 2020, 30(2): 244-251.

Background

FSLLRY-NH2 is an antagonist of the protease-activated receptor 2 (PAR-2) [1]. FSLLRY-NH2 inhibits receptor activation by binding to the external loop 2 (ECL-2) region of PAR-2, thereby blocking protease-induced signal transduction [2]. FSLLRY-NH2 applications in research on inflammation, pruritus, and immune responses [3-4].

In HepG2 cells, FSLLRY-NH2 (100-300μM; 24h) reduces the level of the pro-inflammatory genes IL-8, IL-1b, and TNF-α induced by H_2O_2, through the SAPK/JNK pathways [5]. In A549 cells, FSLLRY-NH2 (100μM; 24h) inhibits PAR2 expression in cells [6].

In asphyxial cardiac arrest (ACA)-induced rat model, FSLLRY-NH2 (50μg; nas; single administration) treatment significantly improved neurological outcomes and reduced the number of degenerating hippocampal neurons after ACA [7]. In Ren-TG mice, FSLLRY-NH2 (10μg/kg; sc; 4 weeks) treatment attenuated the increase in total cardiac mRNA

expression of PAR-2, β-MHC, COL3A1, and TGF-β1 [8].

References:

[1]. Ocasio-Rivera M, Marin-Maldonado F, Trossi-Torres G, et al. Targeting of protease activator receptor-2 (PAR-2) antagonist FSLLRY-NH2 as an asthma adjuvant therapy[J]. Medicine, 2020, 99(43): e22351.
[2]. Hughes K H. Effects of chronic subcutaneous adminstered proteinase-activated receptor 2-activating peptide on vascular reactivity of aortas and blood pressures in mice[D]. Memorial University of Newfoundland, 2011.
[3]. Tsagareli M G, Follansbee T, Iodi Carstens M, et al. Targeting transient receptor potential (TRP) channels, Mas-related G-protein-coupled receptors (Mrgprs), and protease-activated receptors (PARs) to relieve itch[J]. Pharmaceuticals, 2023, 16(12): 1707.
[4]. Weng H J, Pham Q T T, Chang C W, et al. Druggable Targets and Compounds with Both Antinociceptive and Antipruritic Effects[J]. Pharmaceuticals, 2022, 15(7): 892.
[5]. Lee Y J, Kim S J, Kwon K W, et al. Inhibitory effect of FSLLRY-NH2 on inflammatory responses induced by hydrogen peroxide in HepG2 cells[J]. Archives of Pharmacal Research, 2017, 40(7): 854-863.
[6]. Wang B, Wu M D, Lan Y J, et al. PAR2 promotes malignancy in lung adenocarcinoma[J]. American Journal of Translational Research, 2024, 16(12): 7416.
[7]. Ocak U, Ocak P E, Huang L, et al. FSLLRY-NH2 improves neurological outcome after cardiac arrest in rats[J]. Turk Neurosurg, 2020, 30(2): 244-251.
[8]. Narita M, Hanada K, Yokono Y, et al. P938 A direct factor Xa inhibitor, rivaroxaban, attenuates cardiac hypertrophy and fibrosis in renin-overexpressing hypertensive mice[J]. European Heart Journal, 2018, 39(suppl_1): ehy564. P938.