

Product Data Sheet

Product Name: Pep 2-8
 Cat. No.: GC50447

Chemical Properties

Cas. No. 1541011-97-5

Formula C₈₃H₁₁₀N₁₆O₂₄ M.Wt 1715.88

Solubility Soluble 2mg/mL in PBS (pH 7.4) Storage store at -20°C, protect from 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 Ac-Thr-Val-Phe-Thr-Ser-Trp-Glu-Glu-Tyr-Leu-Asp-Trp-Val-NH₂

Protocol

Cell experiment [1]:

Cell lines HepG2 cells

Preparation Method HepG2 cells were seeded at a density of 3×10^4 cells per well in a 96-well plate. After 24 hours, the culture medium was replaced with DMEM medium containing 10% lipoprotein-deficient serum. Different concentrations of Pep 2-8 (1.5, 3.0, 6.0, 12.5, 25, 50, 100, and 200 μM) were pre-incubated with 15 μg/ml PCSK9 (dissolved in 0.5% DMSO) for 30 minutes, and then added to the cells. After 1.5 hours, 10 μg/ml BODIPY-LDL was added and incubated for 3.5 hours. The cells were washed three times with PBS and the fluorescence was measured on a microplate reader.

Reaction Conditions 1.5, 3.0, 6.0, 12.5, 25, 50, 100, and 200 μM; 4h

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Applications Pep 2-8 treatment significantly restored LDL uptake in HepG2 cells.

Animal experiment [2]:

Animal models Male C57BL/6 mice

Preparation Method Male C57BL/6 mice were raised under standard conditions. Before reaching 24 months of age, they were subcutaneously injected with the Pep 2-8 (10µg/kg dissolved in 100µL normal saline) or 100µL normal saline every 2 weeks for a total of 10 weeks (10 mice in each group). After injecting Pep 2-8, the mice were monitored daily. At 24-month endpoint, after euthanizing the mice by CO₂ asphyxiation, the aorta samples were dissected for further molecular and immunohistochemical analyses.

Dosage form 10µg/kg every 2 weeks for 10 weeks; s.c.

Applications Pep 2-8 treatment downregulated the expressions of the aging markers pro-IL-1β, NF-κB and p22^{phox} in the aortic arch of mice.

References:

[1] Zhang Y, Eigenbrot C, Zhou L, et al. Identification of a small peptide that inhibits PCSK9 protein binding to the low density lipoprotein receptor[J]. Journal of Biological Chemistry, 2014, 289(2): 942-955.

[2] Liu S, Wu J, Stolarz A, et al. PCSK9 attenuates efferocytosis in endothelial cells and promotes vascular aging[J]. Theranostics, 2023, 13(9): 2914.

Background

Pep 2-8, a linear peptide consisting of 13 amino acids, inhibits PCSK9 with a K_D value of 0.7µM and suppresses the binding of LDL receptors and the EGF(A) domain to PCSK9, with IC₅₀ values of 0.8 and 0.4µM, respectively [1]. Pep 2-8 neutralizes the activity of PCSK9, prevents the degradation of

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LDL receptors and restore the function of LDL receptors in cells^[2]. Pep 2-8 has been widely used as a model compound to develop a series of derivatives for regulating the level of LDLR protein in cells^[3].

In vitro, Pep 2-8 treatment for 24h (10 μ M) in the presence of lipopolysaccharide (20ng/mL;24h) significantly decreased phosphorylation of mTOR in vascular smooth muscle cells (VSMCs) and decreased apoptosis^[4]. Pep 2-8 (10 μ M) pretreatment of VSMCs from obese insulin-resistant Zucker rats for 30 minutes can inhibit the expression of pERK-1/2 induced by a high glucose environment, and block the activation of the MAPK/ERK-1/2 pathway^[5].

In vivo, Pep 2-8 treatment via subcutaneous injection (10 μ g/kg) once every two weeks for 10 weeks significantly inhibited the downregulation of NOX4, MAPK subunits, and NF- κ B expression caused by PCSK9 in the aorta of mice, as well as the secretion of pro-inflammatory cytokines, preventing vascular aging^[6]. A single intravenous injection of Pep 2-8 (10 μ g/kg) for 120 minutes reduced the myocardial infarction area in rats with ischemia/reperfusion injury, improved the mitochondrial function of the heart, and decreased the expression of apoptosis-related proteins^[7]. Intravenous injection of Pep 2-8 (10 μ g per mouse/day) for one week improved the contractile function of the hearts of mice with left coronary artery (LCA) occlusion and inhibited the autophagic activity in ischemic hearts^[8].

References:

- [1] Zhang Y, Eigenbrot C, Zhou L, et al. Identification of a small peptide that inhibits PCSK9 protein binding to the low density lipoprotein receptor[J]. Journal of Biological Chemistry, 2014, 289(2): 942-955.
- [2] Lammi C, Sgrignani J, Arnoldi A, et al. Biological characterization of computationally designed analogs of peptide TVFTSWEEYLDWV (Pep2-8) with increased PCSK9 antagonistic activity[J]. Scientific reports, 2019, 9(1): 2343.
- [3] Tombling B J, Lammi C, Bollati C, et al. Increased valency improves inhibitory activity of peptides targeting proprotein convertase subtilisin/kexin type 9 (PCSK9)[J]. ChemBioChem, 2021, 22(12): 2154-2160.
- [4] Ding Z, Liu S, Wang X, et al. Cross-talk between PCSK9 and damaged mtDNA in vascular smooth muscle cells: role in apoptosis[J]. Antioxidants & redox signaling, 2016, 25(18): 997-1008.
- [5] Barale C, Tempesta G, Melchionda E, et al. PCSK9 Expression in Vascular Smooth Muscle Cells:

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Role of Insulin Resistance and High Glucose[J]. International Journal of Molecular Sciences, 2025, 26(3): 1003.

[6] Liu S, Wu J, Stolarz A, et al. PCSK9 attenuates efferocytosis in endothelial cells and promotes vascular aging[J]. Theranostics, 2023, 13(9): 2914.

[7] Palee S, McSweeney C M, Maneechote C, et al. PCSK9 inhibitor improves cardiac function and reduces infarct size in rats with ischaemia/reperfusion injury: Benefits beyond lipid-lowering effects[J]. Journal of cellular and molecular medicine, 2019, 23(11): 7310-7319.

[8] Ding Z, Wang X, Liu S, et al. PCSK9 expression in the ischaemic heart and its relationship to infarct size, cardiac function, and development of autophagy[J]. Cardiovascular Research, 2018, 114(13): 1738-1751.

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