

Product Data Sheet

Product Name: cKK-E12
Cat. No.: GC52025

Chemical Properties

Cas. No. 1432494-65-9

SMILES O=C1NC(CCCCN(CC(CCCCCCCCCC)O)CC(CCCCCCCCCC)O)C(NC1CCCCN(CC(CCCCCCCCCC)O)CC(CCCCCCCCCC)O)=O

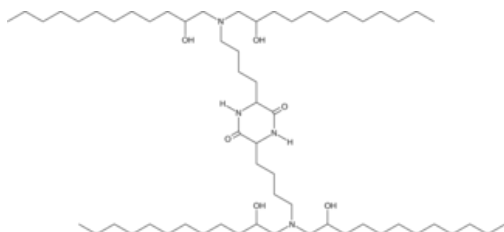
Formula $C_{60}H_{120}N_4O_6$ M.Wt 993.6

Solubility DMSO : 50 mg/mL (50.32 mM; Need ultrasonic) Storage -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 RAW 264.7 macrophages

Preparation Method RAW 264.7 macrophages were treated with cKK-E12 LNP at a dose of 400ng/mL of mRNA for 6h, and the concentrations of pro-inflammatory cytokines (IL-6, TNF- α , IL-1 α , IFN- β) and chemokine MCP-1 in the supernatant were measured using a multiplex cytokine assay.

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

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Reaction Conditions 400ng/mL; 6h

Applications cKK-E12 LNP treatment significantly upregulated the expression of pro-inflammatory cytokines IL-6, TNF- α , IL-1 α , IFN- β and chemokine MCP-1.

Animal experiment [2]:

Animal models C57BL/6 mice

C57BL/6 mice were injected via tail vein with cKK-E12 LNP encapsulating Cy5-labeled mRNA (dose 0.75mg/kg). 1h post-injection, mice were sacrificed, and major organs (liver, spleen, lungs, and kidneys) were harvested and subjected to Preparation Method ex vivo fluorescence imaging using an IVIS imaging system (Ex/Em: 649/670nm). Percent biodistribution was calculated for each organ based on total radiant efficiency analyzed via region of interest using Living Image software.

Dosage form 0.75mg/kg; i.v.

Applications Most cKK-E12 LNP accumulated in the liver (>60%) and, to a lesser extent, the spleen, kidneys, and lungs.

References:

[1] OMO-LAMAI S, WANG Y, PATEL M N, et al. Lipid nanoparticle-associated inflammation is triggered by sensing of endosomal damage: engineering endosomal escape without side effects[J]. bioRxiv, 2024: 2024.04.16.589801.

[2] MELAMED J R, HAJJ K A, CHAUDHARY N, et al. Lipid nanoparticle chemistry determines how nucleoside base modifications alter mRNA delivery[J]. Journal of Controlled Release, 2022, 341: 206-214.

Background

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cKK-E12 is an ionizable lipid that can be used to form lipid nanoparticles (LNP) for efficient delivery of siRNA and mRNA^[1]. LNP formed with cKK-E12 exhibit high surface binding affinity for endogenous apolipoprotein E (ApoE), demonstrating strong tropism for hepatocytes^[2]. cKK-E12 is commonly applied in targeted gene delivery and therapy, vaccine development, molecular imaging, and related fields^[3,4].

In vitro, treatment of RAW 264.7 macrophages with cKK-E12 LNP (400ng/mL) for 6h significantly upregulates the expression of pro-inflammatory cytokines IL-6, TNF- α , IL-1 α , IFN- β , and the chemokine MCP-1. Furthermore, treatment with cKK-E12 LNP (400ng/mL) for 24h markedly increases the proportions of apoptotic, necrotic, and pyroptotic cells^[5].

In vivo, administration of Cy5-labeled mRNA-loaded cKK-E12 LNP (0.75mg/kg) via tail vein injection in C57BL/6 mice results in predominant accumulation in the liver (>60%) within 1h, followed by the spleen, lungs, and kidneys^[6]. Intravenous injection of trastuzumab mRNA-loaded cKK-E12 LNP (0.5, 1, and 2mg/kg) in C57BL/6 mice leads to a dose-dependent increase in serum trastuzumab levels after 24h, reaching approximately 40 μ g/mL at the 2mg/kg dose^[7].

References:

- [1] ZENG Y, ESCALONA-RAYO O, KNOL R, et al. Lipid nanoparticle-based mRNA candidates elicit potent T cell responses[J]. Biomaterials Science, 2023, 11(3): 964-974.
- [2] DONG Y, LOVE K T, DORKIN J R, et al. Lipopeptide nanoparticles for potent and selective siRNA delivery in rodents and nonhuman primates[J]. Proceedings of the National Academy of Sciences, 2014, 111(11): 3955-3960.
- [3] FENTON O S, KAUFFMAN K J, MCCLELLAN R L, et al. Bioinspired alkenyl amino alcohol ionizable lipid materials for highly potent in vivo mRNA delivery[J]. Advanced Materials (Deerfield Beach, Fla.), 2016, 28(15): 2939.
- [4] GORDON A, LI B, WITTEN J, et al. Inhalable dry powders for lung mRNA delivery[J]. Advanced Healthcare Materials, 2024, 13(29): 2400509.
- [5] OMO-LAMAI S, WANG Y, PATEL M N, et al. Lipid nanoparticle-associated inflammation is triggered by sensing of endosomal damage: engineering endosomal escape without side effects[J]. bioRxiv, 2024: 2024.04.16.589801.
- [6] MELAMED J R, HAJJ K A, CHAUDHARY N, et al. Lipid nanoparticle chemistry determines how nucleoside base modifications alter mRNA delivery[J]. Journal of Controlled Release, 2022, 341: 206-214.

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[7] RYBAKOVA Y, KOWALSKI P S, HUANG Y, et al. mRNA delivery for therapeutic anti-HER2 antibody expression in vivo[J]. Molecular Therapy, 2019, 27(8): 1415-1423.

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