Product Data Sheet

Product Name: LGK-974
Cat. No.: GC12392

Chemical Properties

Cas. No.	1243244-14-5		
Chemical Name	2-[5-methyl-6-(2-methylpyridin-4-yl)pyridin-3-yl]-N-(5-pyrazin-2-ylpyridin-2-yl)acetamide		
SMILES	CC1=C(N=CC(=C1)CC(=O)NC2=NC=C(C=C2)C3=NC=CN=C3)C4=CC(=NC=C4)C		
Formula	$C_{23}H_{20}N_6O$	M.Wt	396.44
Solubility	≥ 19.8mg/mL in DMSO	Storage	Store at -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.		

Caution: Product has not been fully validated for medical applications. For research use only.
Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com
Address: 10292 Central Ave. #205, Montclair, CA, USA

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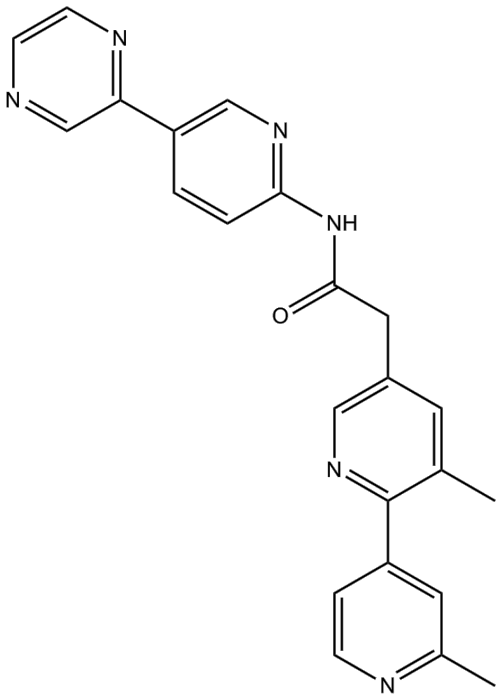
Structure



Protocol

Cell experiment [1]:

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Cell lines	HepG2
Preparation Method	HepG2 cells were treated with 10μM LGK-974 and 4 Gy ionizing radiation for 6h. Then intracellular ROS levels were measured by fluorescence indicator 2,7-dichlorodi-hydrofluorescein diacetate (H2DCFH-DA).
Reaction Conditions	10μM, 6h
Applications	LGK-974 treatment increases the radiosensitivity of HepG2 cells by increasing the level of ROS.

Animal experiment [2]:

Animal models	C57BL/6 mice
Preparation Method	Ischemia/reperfusion (I/R) injury was induced in female C57BL/6 mice aged 10–12 weeks and then were treated with LGK-974 (3mg/kg). Heart tissue samples from the infarct area were collected 2 days after induction of I/R injury, and single-cell suspensions were prepared for flow cytometry analysis.
Dosage form	3mg/kg, 7d, oral
Applications	LGK-974 treatment reduced infiltration of leukocytes and myeloid response following I/R injury.

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References:
[1]. Tian D, Shi Y, Chen D, et al. The Wnt inhibitor LGK-974 enhances radiosensitivity of HepG2 cells by modulating Nrf2 signaling. Int J Oncol. 2017 Aug;51(2):545-554. doi: 10.3892/ijo.2017.4042. Epub 2017 Jun 14. PMID: 28627706.
[2]. Meyer IS, Li X, Meyer C, et al. Blockade of Wnt Secretion Attenuates Myocardial Ischemia-Reperfusion Injury by Modulating the Inflammatory Response. Int J Mol Sci. 2022 Oct 14;23(20):12252. doi: 10.3390/ijms232012252. PMID: 36293109; PMCID: PMC9602582.

Background

LGK-974 is a potent and specific inhibitor of Porcupine (PORCN) [1]. By inhibiting PORCN, LGK-974 effectively inhibits endogenous Wnt/β-catenin signaling, which is critical in various biological processes, including cell proliferation, differentiation, and migration[2]. LGK-974 is commonly utilized in cancer research, particularly in the study of its potential to inhibit tumor growth[3] and modulate the tumor microenvironment[4].

LGK-974 can reduce Wnt-dependent AXIN2 mRNA levels in HN30 cells with an IC_{50} of 0.3nM[5]. In HepG2 cells, treatment with LGK-974 at 10μM for 6h can increase radiosensitivity by elevating reactive oxygen species (ROS) levels[6].

LGK-974 (3mg/kg, 7d, oral) treatment can attenuate the monocytic response and improves the healing process following myocardial infarction in Mice with induced ischemia/reperfusion (I/R) injury[7]. Repeated systemic injections of LGK-974 (2mg/kg, twice daily for 8d, i.p.) can prevent the development of chemotherapy-induced neuropathic pain CINP in rats[8].

References:
[1]. Morgan JT, Raghunathan VK, Chang YR, et al. Wnt inhibition induces persistent increases in intrinsic stiffness of human trabecular meshwork cells. Exp Eye Res. 2015 Mar;132:174-8. doi: 10.1016/j.exer.2015.01.025. Epub 2015 Jan 30. PMID: 25639201; PMCID: PMC4352377.
[2]. Zhang Y, Wang X. Targeting the Wnt/β-catenin signaling pathway in cancer. J Hematol Oncol. 2020 Dec 4;13(1):165. doi: 10.1186/s13045-020-00990-3. PMID: 33276800; PMCID: PMC7716495.
[3]. Guimaraes PPG, Tan M, Tammela T, et al. Potent in vivo lung cancer Wnt signaling inhibition via

cyclodextrin-LGK974 inclusion complexes. J Control Release. 2018 Nov 28;290:75-87. doi: 10.1016/j.jconrel.2018.09.025. Epub 2018 Oct 2. PMID: 30290244; PMCID: PMC6441337.
[4]. Tang Y, Jiang M, Chen A, et al. Porcupine inhibitor LGK-974 inhibits Wnt/β-catenin signaling and modifies tumor-associated macrophages resulting in inhibition of the malignant behaviors of non-small cell lung cancer cells. Mol Med Rep. 2021 Aug;24(2):550. doi: 10.3892/mmr.2021.12189. Epub 2021 Jun 3. PMID: 34080032; PMCID: PMC8185506.
[5]. Liu J, Pan S, Hsieh MH, et al. Targeting Wnt-driven cancer through the inhibition of Porcupine by LGK974. Proc Natl Acad Sci U S A. 2013 Dec 10;110(50):20224-9. doi: 10.1073/pnas.1314239110. Epub 2013 Nov 25. PMID: 24277854; PMCID: PMC3864356.
[6]. Tian D, Shi Y, Chen D, et al. The Wnt inhibitor LGK-974 enhances radiosensitivity of HepG2 cells by modulating Nrf2 signaling. Int J Oncol. 2017 Aug;51(2):545-554. doi: 10.3892/ijo.2017.4042. Epub 2017 Jun 14. PMID: 28627706.
[7]. Meyer IS, Li X, Meyer C, et al. Blockade of Wnt Secretion Attenuates Myocardial Ischemia-Reperfusion Injury by Modulating the Inflammatory Response. Int J Mol Sci. 2022 Oct 14;23(20):12252. doi: 10.3390/ijms232012252. PMID: 36293109; PMCID: PMC9602582.
[8]. Kim HK, Bae J, Lee SH, et al. Blockers of Wnt3a, Wnt10a, or β-Catenin Prevent Chemotherapy-Induced Neuropathic Pain In Vivo. Neurotherapeutics. 2021 Jan;18(1):601-614. doi: 10.1007/s13311-020-00956-w. Epub 2020 Oct 30. PMID: 33128175; PMCID: PMC8116404.