

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 $\geq 19.8\text{mg/mL}$ 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.

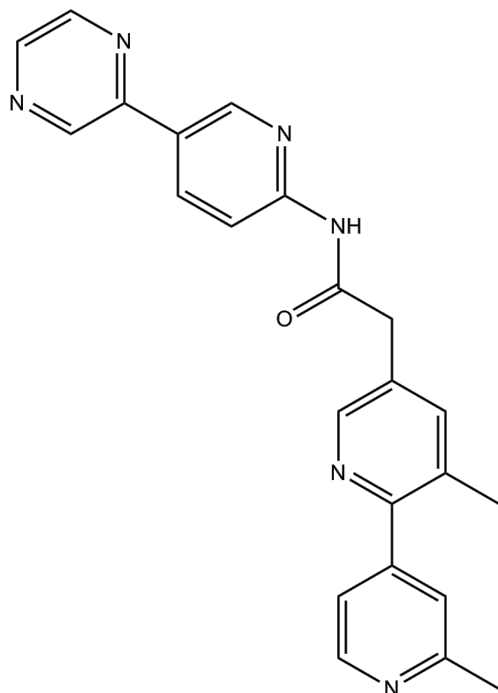
Caution: Product has not been fully validated for medical applications. For research use only.

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

Structure



Protocol

Cell experiment [1]:

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

Product Data Sheet

Cell lines HepG2

HepG2 cells were treated with 10μM LGK-974 and 4 Gy ionizing radiation for Preparation Method 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.

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

Product Data Sheet

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 IC₅₀ of 0.3nM [5]. In HepG2 cells, treatment with LGK-974 at 10 μ M 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

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

Product Data Sheet

- 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.

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