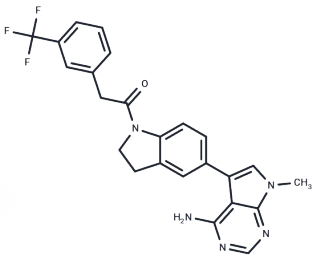
Data Sheet (Cat.No.T2614)

TargetMol

GSK2606414

Chemical Properties



CAS No. : 1337531-36-8

Formula: C24H20F3N5O

Molecular Weight: 451.44

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	GSK2606414 is a cell-permeable and orally active protein kinase R-like endoplasmic reticulum kinase(PERK)inhibitor with IC50 of 0.4 nM. GSK2606414 inhibits PERK activation in cells and suppresses the growth of human tumor xenografts in mice.
Targets(IC50)	Apoptosis,Autophagy,PERK
In vitro	**METHODS**: S1-M1-80 vector and S1-M1-80 sgABCG2 cells were treated with GSK2606414 (0.1, 1, 3, 10, 30, 100 μM, 72 hours), and cytotoxicity was determined by MTT assay. **RESULTS** GSK2606414 showed dose-dependent cytotoxic effects on both cell lines. [2] **METHODS**: N2A cells were treated with GSK2606414 (0.5, 1 μM, 24 hours) and high glucose (30 mM), cells were lysed, and Western blot analysis was performed. **RESULTS** N2A cells treated with GSK2606414 reduced the phosphorylation of eIF2α in cells and significantly reduced p-PERK levels in a dose-dependent manner, and GSK2606414 could inhibit the PERK/p-eIF2α/ATF4/CHOP signaling axis. [3]
In vivo	**METHODS**: GSK2606414 (50, 150 mg/kg, oral, twice a day, 21 days) was used to treat mice bearing subcutaneous pancreatic human BxPC3 tumors and the effect on tumor growth was observed. **RESULTS** GSK2606414 inhibited tumor growth in a dose-dependent manner, with the tumor growth inhibition rates of 20% and 59% at the two doses, respectively. [1]

Solubility Information

Solubility	DMSO: 130 mg/mL (287.97 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 4 mg/mL (8.86 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.2151 mL	11.0757 mL	22.1513 mL
5 mM	0.443 mL	2.2151 mL	4.4303 mL
10 mM	0.2215 mL	1.1076 mL	2.2151 mL
50 mM	0.0443 mL	0.2215 mL	0.443 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Axten JM,et al. Discovery of 7-methyl-5-(1-{[3-(trifluoromethyl)phenyl]acetyl}-2,3-dihydro-1H-indol-5-yl)-7H-pyrrolo[2,3-d]pyrimidin-4-amine (GSK2606414), a potent and selective first-in-class inhibitor of protein kinase R (PKR)-like endoplasmic reticulum kinase (PERK). J Med Chem. 2012 Aug 23;55(16):7193-207.

Guo T, Liu C, Yang C, et al. Immunoproteasome subunit PSMB8 regulates microglia-mediated neuroinflammation upon manganese exposure by PERK signaling. Food and Chemical Toxicology. 2022: 112951.

Yuan J, Yao C, Tang J, et al. Enhanced GRP78 protein expression via the IRE1α/ASK1/p38 MAPK pathway during As2O3-induced endoplasmic reticulum stress in BEAS-2B cells. Toxicology. 2021, 462: 152962.

Yu ZZ, et al. GSK2606414 Sensitizes ABCG2-Overexpressing Multidrug-Resistant Colorectal Cancer Cells to Chemotherapeutic Drugs. Biomedicines. 2023 Nov 20;11(11):3103.

Gundu C, et al. GSK2606414 attenuates PERK/p-eIF2α/ATF4/CHOP axis and augments mitochondrial function to mitigate high glucose induced neurotoxicity in N2A cells. Curr Res Pharmacol Drug Discov. 2022 Jan 24;3:100087.

Meng C, Zhang J, Dang B, et al. PERK pathway activation promotes intracerebral hemorrhage induced secondary brain injury by inducing neuronal apoptosis both in vivo and in vitro. Frontiers in Neuroscience. 2018 Feb 28;12: 111

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