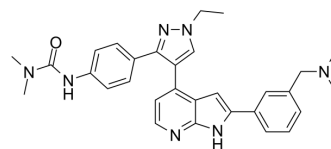


GSK-1070916

Cat. No.:	HY-70044		
CAS No.:	942918-07-2		
Molecular Formula:	C ₃₀ H ₃₃ N ₇ O		
Molecular Weight:	507.63		
Target:	Aurora Kinase; Apoptosis		
Pathway:	Cell Cycle/DNA Damage; Epigenetics; Apoptosis		
Storage:	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	2 years
		-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 16.67 mg/mL (32.84 mM; ultrasonic and warming and heat to 60°C)

Concentration	Solvent	Mass	Preparing Stock Solutions		
			1 mg	5 mg	10 mg
1 mM			1.9699 mL	9.8497 mL	19.6994 mL
5 mM			0.3940 mL	1.9699 mL	3.9399 mL
10 mM			0.1970 mL	0.9850 mL	1.9699 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
Solubility: ≥ 1.67 mg/mL (3.29 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
Solubility: ≥ 1.67 mg/mL (3.29 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil
Solubility: ≥ 1 mg/mL (1.97 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

GSK-1070916 is a potent and selective ATP-competitive inhibitor of aurora B and aurora C with K_is of 0.38 and 1.5 nM, respectively, and is >250- fold selective over Aurora A.

IC₅₀ & Target

Aurora B 0.38 nM (K _i)	Aurora C 1.5 nM (K _i)
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In Vitro

GSK-1070916 potently inhibits Aurora B/INCENP and Aurora C/INCENP kinases with K_is of 0.38±0.29 and 1.45±0.35 nM,

respectively, but is less potent against Aurora A/ TPX2 with a K_i of 492 ± 61 nM. GSK-1070916 also inhibits FLT1, TIE2, SIK, FLT4, and FGFR1 with IC_{50} values of 42, 59, 70, 74, and 78 nM, respectively. Treatment of A549 human lung cancer cells with GSK-1070916 results in a potent antiproliferative effect ($EC_{50} = 7$ nM)^[1]. GSK-1070916 inhibits a panel of tumor cell lines and is shown to inhibit the phosphorylation of HH3-S10 in all cell lines with average EC_{50} values ranging from 8 to 118 nM^[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

In nude mice implanted with human colon tumor (HCT116) xenografts, a single dose of GSK-1070916 administered i.p. inhibits HH3-S10 phosphorylation in a dose-dependent manner. Repeated i.p. administration of GSK-1070916 produces complete or partial antitumor activity in 4 of 8 tumor types [lung, A549; colon, HCT116; acute myelogenous leukemia (AML), HL60; and chronic myelogenous leukemia, K562], stable disease in 3 of 8 (colon, Colo205; lung, H460; and breast, MCF-7), and tumor growth delay in 1 of 8 tumor types (colon, SW620). Daily administration of GSK-1070916 is generally well-tolerated^[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay ^[2]

A panel of tumor cell lines are plated in 96-well plates in the recommended growth media and incubated at 37°C in 5% CO₂ overnight. The following day, the cells are treated with serial dilutions of GSK-1070916. At this time, one set of cells is treated with CellTiter-Glo for a time equal to 0 (T=0) measurement. Following a 6- to 7-d incubation with compound, cell proliferation is measured using the CellTiter-Glo reagent^[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Administration ^[2]

Mice: Tumors are initiated by injection of tumor cell suspensions (A549, SW620, HCT116, H460, MCF-7, HL60, K562) or tumor fragments (Colo205) s.c. into nude (A549, SW620, HCT116, H460, MCF-7, HL60, and Colo205) or severe combined immunodeficient (SCID; K562) mice. When the tumors reach a volume of 80 to 200 mm³, the mice are randomized into groups of 5 to 10 mice per group. GSK-1070916 is administered at 25, 50, or 100 mg/kg once daily for 5 consecutive days-on, 2d-off, schedule for two (Colo205 and HL60) or three (A549, SW620, HCT116, H460, MCF-7, K562) cycles. Tumors are measured twice weekly^[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- J Biomol Screen. 2013 Oct;18(9):1062-71.
- Harvard Medical School LINCS LIBRARY

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REFERENCES

[1]. Adams ND, et al. Discovery of GSK-1070916, a potent and selective inhibitor of Aurora B/C kinase. J Med Chem. 2010 May 27;53(10):3973-4001.

[2]. Hardwicke MA, et al. GSK-1070916, a potent Aurora B/C kinase inhibitor with broad antitumor activity in tissue culture cells and human tumor xenograft models. Mol Cancer Ther. 2009 Jul;8(7):1808-17.

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

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