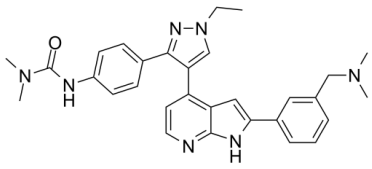
Data Sheet

Product Name:	GSK-1070916
Cat. No.:	CS-0008
CAS No.:	942918-07-2
Molecular Formula:	C30H33N7O
Molecular Weight:	507.63
Target:	Apoptosis; Aurora Kinase
Pathway:	Apoptosis; Cell Cycle/DNA Damage; Epigenetics
Solubility:	DMSO : 10 mg/mL (19.70 mM; Need ultrasonic)



BIOLOGICAL ACTIVITY:

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: Ki: 0.38 nM (Aurora B), 1.5 nM (Aurora C)[1] **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 o inhibits the phosphorylation of HH3- S10 in all cell lines with average EC_{50} values ranging from 8 to 118 nM[2]. **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].

PROTOCOL (Extracted from published papers and Only for reference)

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% CO_2 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]. **Animal Administration:** GSK-1070916 is prepared in 2% Cremophor EL, 2% N,N-dimethylacetamide, and 96% acidified water (pH 5.0)[2].[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 mm^3, 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].

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.

CAIndexNames:

Urea, N'-[4-[4-[2-[3-[(dimethylamino)methyl]phenyl]-1H-pyrrolo[2,3-b]pyridin-4-yl]-1-ethyl-1H-pyrazol-3-yl]phenyl]-N,N-dimethyl-

SMILES:

O=C(NC1=CC=C(C2=NN(C=C2C3=C4C(NC(C5=CC=CC(CN(C)C)=C5)=C4)=NC=C3)CC)C=C1)N(C)C

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