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产品名称：TAK-960
产品别名：TAK-960

生物活性：

Description

TAK-960 is an orally available, selective inhibitor of polo-like kinase 1 (PLK1), with an IC50 of 0.8 nM at 10 μM ATP; TAK-960 also shows inhibitory activities against PLK2 and PLK3, with IC50s of 16.9 and 50.2 nM, respectively.

IC_{50} & Target

PLK1	PLK2	PLK3	FAK/PTK2	MLCK/MYLK	FES/FPS
0.8 nM (IC_{50})	16.9 nM (IC_{50})	50.2 nM (IC_{50})	19.6 nM (IC_{50})	25.6 nM (IC_{50})	58.2 nM (IC_{50})

In Vitro

TAK-960 inhibits full-length PLK1 protein with IC50 of 0.8 nM, wich is 20-fold lower than the next lowest IC50 value (PLK2: 16.9 nM). TAK-960 (2-1000 nM) causes accumulation of G2-M cells in HT-29 cells. TAK-960 inhibits proliferation of multiple cancer cell lines, with mean EC50 values ranging from 8.4 to 46.9 nM, but not in nondividing normal cells[1]. TAK-960 (8 nM) leads to G2/M cell cycle arrest without significant cytotoxicity in HeLa cells. TAK-960 does not sensitize cancer cells to radiation when an insufficient amount of time is provided to induce mitotic arrest. The overexpression of a PLK1 mutant, PLK1-R136G&T210D, which is confirmed to cancel the TAK-960-mediated increase in the proportion of mitotic cells, abrogates the radiosensitizing effects of TAK-960[2].

In Vivo

TAK-960 (7.5 mg/kg, p.o.) shows a significant increase in median survival compared with vehicle in MV4-11 human leukemia model. TAK-960 (10 mg/kg, p.o.) inhibits tumor growth in the MDR1-expressing K562ADR-bearing leukemia xenograft model[1]. TAK-960 (10 mg/kg) significantly suppresses tumor growth when combined with IR in tumor xenografts[2].

Solvent&Solubility

In Vitro:

DMSO : ≥ 35 mg/mL (62.32 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7806 mL	8.9031 mL	17.8063 mL
	5 mM	0.3561 mL	1.7806 mL	3.5613 mL
	10 mM	0.1781 mL	0.8903 mL	1.7806 mL

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

References

[1]. Hikichi Y, et al. TAK-960, a novel, orally available, selective inhibitor of polo-like kinase 1, shows broad-spectrum preclinical antitumor activity in multiple dosing regimens. Mol Cancer Ther. 2012 Mar;11(3):700-9.

[2]. Inoue M, et al. PLK1 blockade enhances therapeutic effects of radiation by inducing cell cycle arrest at the mitotic phase. Sci Rep. 2015 Oct 27;5:15666.

实验参考：

Cell Assay	Cells are seeded into 96-well plates at 3,000 to 30,000 cells per well in appropriate medium plus 10% fetal calf serum. After 24 hours, cells are treated with serial dilutions of TAK-960, and 72 hours later, the number of viable cells is assessed using the CellTiter-Glo Assay. Calculation of EC50 values and statistical analysis are done using GraphPad Prism software. [1]
Animal Administration	The suspension of HeLa cells (2×10^6 in 100 μL PBS) or H1299 cells (3×10^6 in 100 μL PBS) is subcutaneously inoculated into the right hind legs of 8-week-old nude mice (BALB/c nu/nu mice). The indicated dose of TAK-960 is orally administered to tumor-bearing mice. In the radiation treatment, tumor xenografts are locally irradiated with the indicated dose of ^{137}Cs γ-rays using a Gammacell 40 Exactor. [2]
Kinase Assay	The inhibitory activity of TAK-960 is assessed by the TR-FRET (fluorescence resonance energy transfer) assay, which measures the ATP-dependent phosphorylation of a biotinylated substrate peptide corresponding to residues 2,470 through 2,488 of the mTOR protein (Biotin-AGAGTVPESIHSFIGDGLV). A total of 288 kinases are screened for TAK-960 inhibition (1 μM) using HotSpot technology and IC50 values for the selected kinases are determined. [1]
References	[1]. Hikichi Y, et al. TAK-960, a novel, orally available, selective inhibitor of polo-like kinase 1, shows broad-spectrum preclinical antitumor activity in multiple dosing regimens. Mol Cancer Ther. 2012 Mar;11(3):700-9. [2]. Inoue M, et al. PLK1 blockade enhances therapeutic effects of radiation by inducing cell cycle arrest at the mitotic phase. Sci Rep. 2015 Oct 27;5:15666.