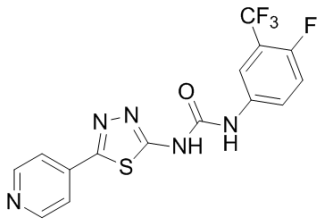
ML216

Cat. No.:	HY-12342
CAS No.:	1430213-30-1
Molecular Formula:	$C_{15}H_9F_4N_5OS$
Molecular Weight:	383.32
Target:	DNA/RNA Synthesis
Pathway:	Cell Cycle/DNA Damage
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 20 mg/mL (52.18 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.6088 mL	13.0439 mL	26.0879 mL
5 mM	0.5218 mL	2.6088 mL	5.2176 mL
10 mM	0.2609 mL	1.3044 mL	2.6088 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2 mg/mL (5.22 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

ML216 (CID-49852229) is a potent, selective and cell permeable inhibitor of the DNA unwinding activity of BLM helicase with IC_{50}s of 2.98 μM and 0.97 μM for $BLM^{full\text{-}length}$ and $BLM^{636\text{-}1298}$, respectively. ML216 inhibits ssDNA-dependent ATPase activity of BLM with a K_i of 1.76 μM. Antitumor avtivity[1][2].

IC_{50} & Target

IC50: 2.98 μM ($BLM^{full\text{-}length}$) and 0.97 μM ($BLM^{636\text{-}1298}$)[1]

In Vitro

ML216 (12.5-50 μM; 24-72 hours; PSNG5 and PSNG13cells) treatment inhibits the proliferation of PSNF5 cells in a concentration-dependent manner, but not of PSNG13 cells[1].
ML216 treatment leads to a statistically significant increase in the frequency of sister chromatid exchanges (SCEs) in PSNF5 cells, but not in PSNG13 cells[1].
ML216 increases the sensitivity of PSNF5 cells to aphidicolin but has no sensitizing effect on isogenic PSNG13 cells devoid of BLM[1].

ML216 inhibits both the full length WRN (IC_{50} of 5 μM) and a truncated $WRN^{500-946}$ (IC_{50} of 12.6 μM), with the former being 2.5-fold more sensitive to inhibition. BLM is a little more sensitive than WRN to inhibition by ML216 (1.7-fold based on IC_{50} values). Despite the detectable inhibition of WRN by ML216, this compound appears selective for BLM in human cells. ML216 inhibits proliferation of WRN^{+} and WRN^{-} cells equally well, and similarly sensitized both cell types to aphidicolin[1].

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

Cell Proliferation Assay[1]

Cell Line:	PSNG5 and PSNG13cells
Concentration:	12.5 μM or 50 μM
Incubation Time:	24 hours, 48 hours, 72 hours
Result:	Inhibited the proliferation of PSNF5 cells, but not of PSNG13 cells, and did so in a concentration-dependent manner.

In Vivo

Although ML216 inhibits unwinding by the sequence-related BLM and WRN helicases similarly in vitro, the apparent dependence on BLM for ML216 to exert its biological effects in human cells suggests BLM specificity for the drug's mechanism of action in vivo. A co-crystal structure of BLM in complex with inhibitor would be informative. Cellular cues in vivo may induce a specific conformation of WRN that makes it resistant to ML216[2].

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CUSTOMER VALIDATION

- Am J Cancer Res. 2021 Apr 15;11(4):1347-1368.

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REFERENCES

[1]. Nguyen GH, et al. A small molecule inhibitor of the BLM helicase modulates chromosome stability in human cells. Chem Biol. 2013 Jan 24;20(1):55-62.

[2]. Banerjee T, et al. A new development in DNA repair modulation: discovery of a BLM helicase inhibitor. Cell Cycle. 2013 Mar 1;12(5):713-4.

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