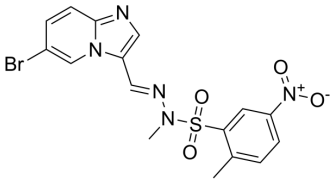
PIK-75

Cat. No.:	HY-107834
CAS No.:	372196-67-3
Molecular Formula:	$C_{16}H_{14}BrN_5O_4S$
Molecular Weight:	452.28
Target:	DNA-PK; PI3K; Apoptosis
Pathway:	Cell Cycle/DNA Damage; PI3K/Akt/mTOR; Apoptosis
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

PIK-75 is a reversible DNA-PK and p110α-selective inhibitor, which inhibits DNA-PK, p110α and p110γ with IC_{50}s of 2, 5.8 and 76 nM, respectively. PIK-75 inhibits p110α >200-fold more potently than p110β (IC_{50}=1.3 μM)[1][2]. PIK-75 induces apoptosis [3].

IC_{50} & Target

DNA-PK 2 nM (IC_{50})	p110α 5.8 nM (IC_{50})	p110γ 76 nM (IC_{50})	p110δ 510 nM (IC_{50})
p110β 1.3 μM (IC_{50})	hsVPS34 2.6 μM (IC_{50})	PI3KC2β 1 μM (IC_{50})	PI3KC2α 10 μM (IC_{50})
mTORC1 1 μM (IC_{50})	mTORC2 10 μM (IC_{50})	ATM 2.3 μM (IC_{50})	ATR 21 μM (IC_{50})
PI4KIIIβ 50 μM (IC_{50})			

In Vitro

PIK-75 also inhibits p110δ, PI3KC2β, mTORC1, ATM, hsVPS34, PI3KC2α, mTORC2, ATR and PI4KIIIβ with IC_{50}s of 510 nM, ~1 μM, ~1 μM, 2.3 μM, 2.6 μM, ~10 μM, ~10 μM, 21 μM, ~50 μM, respectively[1].

PIK-75 alone blocks Thr 308 phosphorylation in L6 myotubes and 3T3-L1 adipocytes with IC_{50} values of 1.2 and 1.3 μM, respectively[1].

PIK-75 (1-1000 nM; 5 min) blocks the phosphorylation of PKB induced by insulin on both Ser473and Thr308 in CHO-IR cells in a dose-dependent manner, with an IC_{50} of 78 nM[2].

PIK-75 (0.1-1000 nM; 48 hours) inhibits the proliferation and survival of pancreatic cancer cells through apoptotic cell death [3].

PIK-75 (0.1-1000 nM) also reduces the colony formation of pancreatic cancer MIA PaCa-2 and AsPC-1 cells[3].

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

Cell Viability Assay[3]

Cell Line:	Human pancreatic cancer cells (MIA PaCa-2 or AsPC-1)
Concentration:	0.1, 0.3, 1, 3, 10, 30, 100, 300, and 1000 nM
Incubation Time:	48 hours

Result:	Submicromolar concentration was sufficient to inhibit the proliferation of pancreatic cancer, MIA PaCa-2 and AsPC-1 cells after 48-h treatment.

Western Blot Analysis[2]

Cell Line:	Overnight-starved CHO-IR cells
Concentration:	1, 10, 100, 1000 nM
Incubation Time:	5 minutes
Result:	Blocked the phosphorylation of PKB induced by insulin (1 nM, 10 min) on both Ser473and Thr308 in a dose-dependent manner.PIK-75 potentiates anticancer activity of Gemcitabine (20 mg/kg) in vivo. Gemcitabine (20 mg/kg) or PIK-75 (2 mg/kg) alone reduces the tumor growth to similar degree. Beneficial effect of PIK-75/Gemcitabine is evident as this combination markedly reduces the tumor growth in vivowithout affecting the body weights of mice[3].

In Vivo

PIK-75 (2 mg/kg) potentiates anticancer activity of Gemcitabine (20 mg/kg) in vivo. Gemcitabine (20 mg/kg) or PIK-75 (2 mg/kg) alone reduces the tumor growth to similar degree. Beneficial effect of PIK-75/Gemcitabine is evident as this combination markedly reduces the tumor growth in vivowithout affecting the body weights of mice[3].

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Animal Model:	Mice bearing tumors of MIA PaCa-2[3]
Dosage:	2 mg/kg; or combination with Gemcitabine (20 mg/kg)
Administration:	Administered injection; 5 times per week. 25 days
Result:	Reduced the tumor growth and enhanced the antitumor effect.

CUSTOMER VALIDATION

- Clin Cancer Res. 2020 Apr 15;26(8):2011-2021.
- Molecules. 2020 Apr 23;25(8):1980.

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REFERENCES

[1]. Knight ZA, et al. A pharmacological map of the PI3-K family defines a role for p110alpha in insulin signaling. Cell. 2006 May 19;125(4):733-47.

[2]. Chaussade C, et al. Evidence for functional redundancy of class IA PI3K isoforms in insulin signalling. Biochem J. 2007 Jun 15;404(3):449-58.

[3]. Duong HQ, et al. Inhibition of NRF2 by PIK-75 augments sensitivity of pancreatic cancer cells to gemcitabine. Int J Oncol. 2014 Mar;44(3):959-69.

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

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