Small Molecules

NU7441

NHEJ pathway inhibitor; Inhibits DNA-dependent protein kinase (DNA-PK)

Catalog #	74082	5 mg
	74084	10 mg

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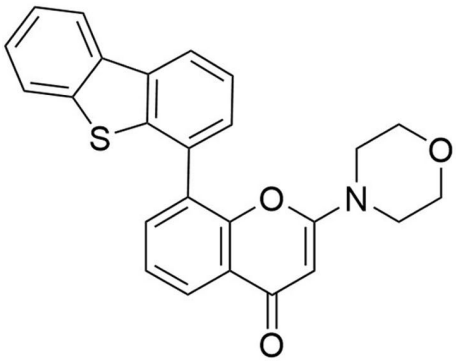
Product Description

NU7441 is an inhibitor of DNA-dependent protein kinase (DNA-PK), an enzyme involved in the non-homologous end joining (NHEJ) DNA repair pathway. It is highly selective for DNA-PK, with an IC_{50} of 14 nM (Leahy et al.).

Molecular Name:	NU7441
Alternative Names:	KU57788
CAS Number:	503468-95-9
Chemical Formula:	$C_{25}H_{19}NO_3S$
Molecular Weight:	413.5 g/mol
Purity:	≥ 98%
Chemical Name:	8-(4-dibenzothienyl)-2-(4-morpholinyl)-4H-1-benzopyran-4-one
Structure:	

Properties

Physical Appearance:	A crystalline solid
Storage:	Product stable at -20°C as supplied. Protect product from prolonged exposure to light. For long-term storage, store with a desiccant. Stable as supplied for 12 months from date of receipt.
Solubility:	· DMSO ≤ 290 µM · DMF ≤ 2.4 mM For example, to prepare a 1 mM stock solution in DMF, resuspend 1 mg in 2.42 mL of DMF. Prepare stock solution fresh before use. Information regarding stability of small molecules in solution has rarely been reported, however, as a general guide we recommend storage in DMF at -20°C. Aliquot into working volumes to avoid repeated freeze-thaw cycles. The effect of storage of stock solution on compound performance should be tested for each application. Compound has low solubility in aqueous media. For use as a cell culture supplement, stock solution should be diluted into culture medium immediately before use. Avoid final DMF concentration above 0.1% due to potential cell toxicity.

Published Applications

GENOME EDITING
· Reduces the frequency of NHEJ and increases the efficiency of homology-directed repair (HDR) in CRISPR-Cas9 genome editing (Robert et al.).
CANCER RESEARCH
· Sensitizes human cancer cell lines to DNA double-strand-break-inducing therapies (chemo- or radio-therapy) by inhibiting DNA-PK activity and delaying the repair of double-strand breaks (Ciszewski et al.; Shaheen et al.; Yang et al.; Zhao et al.).

References

Ciszewski WM et al. (2014) DNA-PK inhibition by NU7441 sensitizes breast cancer cells to ionizing radiation and doxorubicin. Breast Cancer Res Treat 143(1): 47–55.
Leahy JJ et al. (2004) Identification of a highly potent and selective DNA-dependent protein kinase (DNA-PK) inhibitor (NU7441) by screening of chromenone libraries. Bioorg Med Chem Lett 14(24): 6083–7.
Robert F et al. (2015) Pharmacological inhibition of DNA-PK stimulates Cas9-mediated genome editing. Genome Med 7(1): 93.
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Yang C et al. (2016) NU7441 enhances the radiosensitivity of liver cancer cells. Cell Physiol Biochem 38(5): 1897–905.
Zhao Y et al. (2006) Preclinical evaluation of a potent novel DNA-dependent protein kinase inhibitor NU7441. Cancer Res 66(10): 5354–62.

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