Small Molecules

KU0060648

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

Catalog #	74062	10 mg
	74064	25 mg

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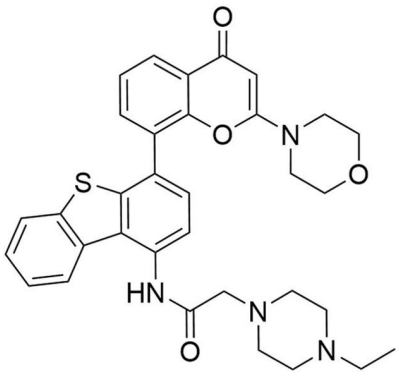
Product Description

KU0060648 is an ATP-competitive and highly potent inhibitor of DNA-dependent protein kinase (DNA-PK), with IC_{50} values of 19 nM in MCF7 human breast cancer cells and 170 nM in SW620 human colon cancer cells. KU0060648 also inhibits phosphoinositide 3-kinase (PI3K) with IC_{50} values of 39 nM in MCF7 cells and > 10 µM in SW620 cells, which suggests a cell-dependent mechanism (Munck et al.).

Molecular Name:	KU0060648
Alternative Names:	Not applicable
CAS Number:	881375-00-4
Chemical Formula:	$C_{33}H_{34}N_4O_4S$
Molecular Weight:	582.7 g/mol
Purity:	≥ 98%
Chemical Name:	2-(4-ethylpiperazin-1-yl)-N-[4-(2-morpholin-4-yl-4-oxochromen-8-yl)dibenzothiophen-1-yl]acetamide
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 ≤ 1.7 mM For example, to prepare a 1 mM stock solution in DMSO, resuspend 10 mg in 17 mL of DMSO. 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 DMSO 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 DMSO concentration above 0.1% due to potential cell toxicity.

Published Applications

GENOME EDITING
· Reduces the frequency of non-homologous end joining (NHEJ) and increases the efficiency of homology-directed repair (HDR) in CRISPR-Cas9 genome editing (Robert et al.).
CANCER RESEARCH
· Inhibits tumor growth and sensitizes human cancer cells to DNA double-strand-break (DSB)-inducing therapies (chemo- or radio-therapy) by inhibiting both DNA-PK and PI3K and preventing the execution of DSB repair (Chen et al.; Dietlein et al.; Munck et al.).

References

Chen M-B et al. (2016) KU-0060648 inhibits hepatocellular carcinoma cells through DNA-PKcs-dependent and DNA-PKcs-independent mechanisms. Oncotarget 7(13): 17047–59.
Dietlein F et al. (2014) Cancer-specific defects in DNA repair pathways as targets for personalized therapeutic approaches. Trends Genet 30(8): 326–39.
Munck JM et al. (2012) Chemosensitization of cancer cells by KU-0060648, a dual inhibitor of DNA-PK and PI-3K. Mol Cancer Ther 11(8): 1789–98.
Robert F et al. (2015) Pharmacological inhibition of DNA-PK stimulates Cas9-mediated genome editing. Genome Med 7: 93.

Related Small Molecules

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This product is hazardous. Please refer to the Safety Data Sheet (SDS).