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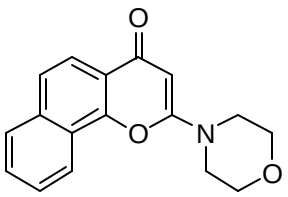
ProductInformation

NU7026

Catalog Number **N 1537**
Storage Temperature 2-8 °C

CAS RN: 154447-35-5

Synonym: 2-(Morpholin-4-yl)-benzo[h]chomen-4-one



Product Description
Molecular Formula: $C_{17}H_{15}NO_3$
Molecular Weight: 281.31

NU7026 is a cell permeable small molecule benzochromenone inhibitor of DNA repair enzyme DNA-dependent protein kinase (DNA-PK). DNA-PK is implicated in SCID & Werner's syndromes, breast cancer, sensitivity to irradiation and genomic instability. DNA-PK functions in double-stranded break NHEJ (nonhomologous end joining) DNA repair[1] and in V(D)J recombination for antigen recognition region of Ig genes.[2]

NU7026 inhibits DNA-PK with an IC_{50} = 0.23 µM in an ATP-competitive manner. It exhibits selectivity over other PI3K-related kinases (IC_{50} = 13 µM for PI3K and >100 µM for ATM and ATR).[1] It inhibits DNA-PK-mediated, but not PARP-1-mediated, DNA double-strand breaks (DSBs) repair. DNA-PK mediates NHEJ DNA repair. Inhibition of this DSB repair pathway may sensitize cells to topoisomerase II poisons. NU7026 potentiates topo II poisons through inhibition of NHEJ and a G2/M checkpoint arrest. This identifies DNA-PK as a potential target for leukemia therapy.[3] NU7026, at 10 µM, potentiated IR cytotoxicity (potentiation factor at 90% cell kill , PF_{90} = 1.51 +/- 0.04) in exponentially growing DNA-PK proficient cells, while PARP-1 inhibitor AG14361 at 0.4 µM, potentiated IR in PARP-1(+/+) (PF_{90} = 1.37 +/- 0.03) but not PARP-1(-/-) cells. When NU7026 and AG14361 were used in combination, their potentiating effects were additive (e.g., PF_{90} = 2.81 +/- 0.19) in PARP-1(+/+) cells. Thus, the DNA-PK and PARP-1 inhibitors act as potent radiosensitizers and show potential as tools for anticancer therapeutic intervention.[1]

Precautions and Disclaimer
This product is for R&D use only, not for drug, household, or other uses. Please consult the Material Safety Data Sheet for information regarding hazards and safe handling practices.

Preparation Instructions
NU7026 is soluble in DMSO at 3 mg/mL with warming to 60 °C. It is insoluble in water.

Storage/Stability
Store NU7026 at 2-8 °C.

References
1. Veuger S. J., et al., Radiosensitization and DNA repair inhibition by the combined use of novel inhibitors of DNA-dependent protein kinase and poly(ADP-ribose) polymerase-1. *Cancer Res.*, **63**, 6008-6015 (2003).
2. Hollick, J. J. et al., 2,6-disubstituted pyran-4-one and thiopyran-4-one inhibitors of DNA-Dependent protein kinase (DNA-PK). *Bioorg. Med. Chem. Lett.*, **13**, 3083-3086 (2003).
3. Willmore, E., et al., A novel DNA-dependent protein kinase inhibitor, NU7026, potentiates the cytotoxicity of topoisomerase II poisons used in the treatment of leukemia. *Blood*, **103**, 4659-4665 (2004).

AH,PHC 11/05-1

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