DNA-PK-IN-13

Cat. No.: HY-158166

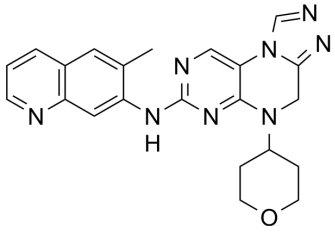
Molecular Formula: $C_{22}H_{22}N_8O$

Molecular Weight: 414.46

Target: DNA-PK

Pathway: Cell Cycle/DNA Damage; PI3K/Akt/mTOR

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

DNA-PK-IN-13 (Compound SK10) is a DNA-PK inhibitor that exhibits potent inhibitory activity (IC_{50}= 0.11 nM). DNA-PK-IN-13 regulates tumor cell proliferation by decreasing the expression level of γH2A.X and enhancing the sensitivity of tumor cells to chemotherapeutic agents. DNA-PK-IN-13 is suitable for oncology studies[1].

In Vitro

DNA-PK-IN-13 displays the best antiproliferative activities with IC_{50} values of 0.6 μM against Jurkat T-cell[1].

DNA-PK-IN-13 (0.1-40 μM; 10 min) concentration-dependently decreases the expression level of γH2A.X in Jurkat cells and HepG2 cells[1].

DNA-PK-IN-13 (1 μM; 24 hours) in combination with doxorubicin (HY-15142A) (0.1 μM) results in a significant decrease in the proportion of S-phase and an increase in the proportion of G2/M-phase in the Jurkat cell[1].

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

Western Blot Analysis[1]

Cell Line:	HepG2 cells, Jurkat cells
Concentration:	0.1; 0.5; 5; 10; 20; 40μM
Incubation Time:	10min
Result:	Concentration-dependently decreased the expression level of γH2A.X in Jurkat cells and HepG2 cells. DNA-PK-IN-13 can affect the production of γH2A.X and thus inhibit DNA damage repair.

Cell Cycle Analysis[1]

Cell Line:	Jurkat cells
Concentration:	1μM; Dox 0.1μM
Incubation Time:	24h
Result:	DNA-PK-IN-13 alone did not demonstrate statistically significant differences in the cell cycle. However, when combined with doxorubicin, DNA-PK-IN-13 influenced the cell cycle, contributing to cell death.

In Vivo

DNA-PK-IN-13 has good oral bioavailability (F = 31.8%)[1].

Pharmacokinetic Analysis in DNA-PK-IN-13[1]

Route	Dose (mg/kg)	AUC_{0-t} (ug/L·h)	$AUC_{0-\infty}$ (ug/L·h)	$t_{1/2}$ (h)	T_{max} (h)	Cl (L/h/kg)	V_z (L/kg)	C_0 (ug/L)	C_{max} (ug/L)	F (%)
i.v.	2	604.4 ± 61.6	605.4 ± 61.9	1.0 ± 0.4	0.083	3.3 ± 0.3	4.7 ± 1.9	1003.9 ± 201.8	NA	/
p.o.	10	949.5 ± 405.2	962.3 ± 412.1	2.0 ± 0.6	1.4 ± 1.1	12.6 ± 7.4	38.8 ± 30.2	NA	324.1 ± 149.0	31.8

DNA-PK-IN-13 (i.p.; 10 mg/kg; single dose) has tumor suppressor activity in CT26 colon cancer mice.Co-administration with doxorubicin (2.5 mg/kg) is effective and safe[1].

DNA-PK-IN-13 (i.p.; 10 mg/kg; 13 consecutive days) in combination with PD-1/PD-L1 inhibitors inhibits tumor growth more significantly[1].

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

Animal Model:	CT26 colon cancer mouse [1]
Dosage:	10 mg/kg single dose
Administration:	i.p
Result:	Single-agent treatment reduced tumor weight by 30.8% and tumor volume by 32.1%. Co-administration with doxorubicin (2.5 mg/kg) produced more significant tumor inhibitory activity, with a TGI of 50.2%. No significant weight loss or deaths were observed.

REFERENCES

[1]. Cheng B, Y et al. Discovery of Novel Heterotricyclic Compounds as DNA-Dependent Protein Kinase (DNA-PK) Inhibitors with Enhanced Chemosensitivity, Oral Bioavailability, and the Ability to Potentiate Cancer Immunotherapy. J Med Chem. 2024 Apr 25;67(8):6253-6267

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