LL-K8-22

Cat. No.: HY-149209

Molecular Formula: $C_{37}H_{43}N_5O$

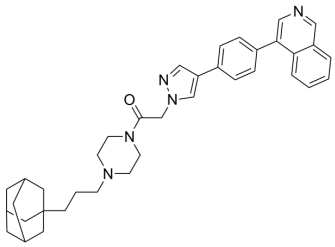
Molecular Weight: 573.77

Target: CDK; STAT; Early 2 Factor (E2F)

Pathway: Cell Cycle/DNA Damage; JAK/STAT Signaling; Stem Cell/Wnt

Storage:

Powder	-20°C	3 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 125 mg/mL (217.86 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.7429 mL	8.7143 mL	17.4286 mL
5 mM	0.3486 mL	1.7429 mL	3.4857 mL
10 mM	0.1743 mL	0.8714 mL	1.7429 mL

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description

LL-K8-22 is a potent, selective and durable CDK8-cyclin C dual degrader, with DC_{50} values of 2.52 and 2.64 μM, respectively. LL-K8-22 also suppresses STAT1 Ser 727 phosphorylation. LL-K8-22 inhibits E2F- and MYC-driven carcinogenic transcriptional programs. LL-K8-22 can be used for triplenegative breast cancer (TNBC) research[1].

IC_{50} & Target

CDK8 2.52 μM (DC50)	STAT1

In Vitro

LL-K8-22 (0-10 μM, 24 h) degrades the CDK8-cyclin C complex in a dose-dependent manner[1].
LL-K8-22 (0-20 μM, 4 days) suppresses tumor cell proliferation[1].
LL-K8-22 (0-8 μM, 24 h) inhibits CDK8-cyclin C downstream signaling[1].
LL-K8-22 significantly downregulated EAPP (E2F family binding protein)[1].
LL-K8-22 dose not affect CDK8 and CCNC mRNA levels[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[1]

Cell Line:	MDA-MB-468 cells

Concentration:	0, 0.625, 1.25, 2.5, 5, and 10 μM
Incubation Time:	24 h
Result:	Induced selective and synchronous degradation of CDK8 and cyclin C protein expression in a dose-dependent manner with DC_{50} of 2.52 and 2.64 μM, respectively. Significantly degraded CDK8 without reducing CDK19 (a highly homologous protein of CDK8) and did not degrade other cyclin proteins except cyclin C.

Cell Proliferation Assay[1]

Cell Line:	MDA-MB-468, HCT-116, and MDA-MB-231 cells
Concentration:	0, 0.625, 1.25, 2.5, 5, and 10 μM
Incubation Time:	24 h
Result:	Induced selective and synchronous degradation of CDK8 and cyclin C protein expression in a dose-dependent manner with DC_{50} of 2.52 and 2.64 μM, respectively. Significantly degraded CDK8 without reducing CDK19 (a highly homologous protein of CDK8) and did not degrade other cyclin proteins except cyclin C.

Western Blot Analysis[1]

Cell Line:	MDA-MB-468 cells
Concentration:	0, 2, 4, and 8 μM
Incubation Time:	24 h
Result:	Reduced Ser 2 and Ser 5 phosphorylation of the C-terminal domain of RNA pol II in adose-dependent manner. Only inhibited the Ser 727 phosphorylation of STAT1 and did not affect Janus kinase (JAK)-mediated phosphorylation of Tyr 701.

REFERENCES

[1]. Wang M, et al. Discovery of LL-K8-22: A Selective, Durable, and Small-Molecule Degrader of the CDK8-Cyclin C Complex. J Med Chem. 2023 Apr 13;66(7):4932-4951.

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