HTH-01-091

Cat. No.: HY-122665

CAS No.: 2000209-42-5

Molecular Formula: $C_{26}H_{28}Cl_2N_4O_2$

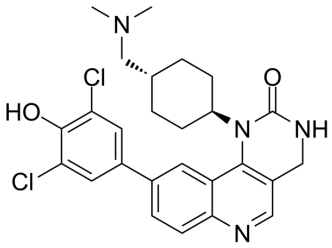
Molecular Weight: 499

Target: MELK; DYRK; Pim; mTOR; CDK; GSK-3; RIP kinase

Pathway: PI3K/Akt/mTOR; Protein Tyrosine Kinase/RTK; JAK/STAT Signaling; Cell Cycle/DNA Damage; Stem Cell/Wnt; Apoptosis

Storage:

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



BIOLOGICAL ACTIVITY

Description

HTH-01-091 is a potent and selective maternal embryonic leucine zipper kinase (MELK) inhibitor, with an IC_{50} of 10.5 nM. HTH-01-091 also inhibits PIM1/2/3, RIPK2, DYRK3, smMLCK and CLK2. HTH-01-091 can be uesd for breast cancer research[1].

IC_{50} & Target

DYRK4 41.8 nM (IC_{50})	PIM1 60.6 nM (IC_{50})	mTOR 632 nM (IC_{50})	CDK7 1230 nM (IC_{50})
PIM2	PIM3		

In Vitro

HTH-01-091 (1 μM) selectively inhibits 4% of the kinases over 90%[1].
HTH-01-091 (0-10 μM, 1 h) is cell permeable and causes MELK degradation[1].
HTH-01-091 (0-10 μM, 3 day) exhibits minor antiproliferative effects in breast cancer cells[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, 0.1, 1.0, and 10 μM
Incubation Time:	1 h
Result:	Reduced MELK protein levels in MDA-MB-468 cells; Dose-dependently decreased MELK pull-down by streptavidin beads, demonstrating that the compound is cell permeable and binds to MELK in an ATP-competitive fashion. Had no effect on ERK1/2 pull-down, showing no binding affinity of HTH-01-091 to ERK1/2.

Cell Proliferation Assay[1]

Cell Line:	MDA-MB-468, BT-549, HCC70, ZR-75-1, MCF7, and T-47D cells
Concentration:	0, 0.001, 0.01, 0.1, 1.0, and 10 μM
Incubation Time:	3 day

Result:	Showed antiproliferative activities in a panel of breast cancer cell lines, including MDA-MB-468, BT-549, HCC70, ZR-75-1, MCF7, and T-47D cells, with IC_{50} values of 4.00 μM, 6.16 μM, 8.80 μM, >10 μM, 8.75 μM, and 3.87 μM, respectively.

REFERENCES

[1]. Huang HT, et al. MELK is not necessary for the proliferation of basal-like breast cancer cells. Elife. 2017 Sep 19;6:e26693.

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