HTH-01-091 TFA

Cat. No.: HY-122665A

Molecular Formula: $C_{28}H_{29}Cl_2F_3N_4O_4$

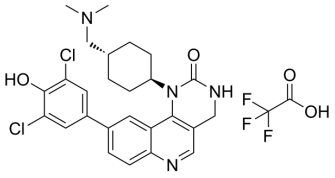
Molecular Weight: 613.46

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
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (163.01 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.6301 mL	8.1505 mL	16.3010 mL
	5 mM	0.3260 mL	1.6301 mL	3.2602 mL
	10 mM	0.1630 mL	0.8150 mL	1.6301 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (4.08 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.08 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.08 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

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

IC_{50} & Target

IC50: 10.5 nM (MELK), 41.8 nM (DYRK3), 42.5 nM (RIPK2), 60.6 nM (PIM1), 108.6 nM (smMLCK), 632 nM (mTOR), 962 nM (PIK3CA), 1230 nM (CDK7), 1740 nM (GSK3A)[1]

In Vitro

HTH-01-091 (1 μM) TFA selectively inhibits 4% of the kinases over 90%[1].

HTH-01-091 (0-10 μM, 1 h) TFA is cell permeable and causes MELK degradation[1].
HTH-01-091 (0-10 μM, 3 day) TFA exhibits minor antiproliferative effects in breast cancer cells[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

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.

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.

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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