HI-TOPK-032

Cat. No.: HY-101550

CAS No.: 487020-03-1

Molecular Formula: $C_{20}H_{11}N_5OS$

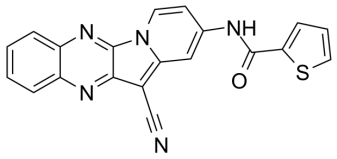
Molecular Weight: 369.4

Target: TOPK

Pathway: Cell Cycle/DNA Damage

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 2.5 mg/mL (6.77 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.7071 mL	13.5355 mL	27.0709 mL
	5 mM	0.5414 mL	2.7071 mL	5.4142 mL
	10 mM	---	---	---

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

In Vivo

1. Add each solvent one by one: 15% Cremophor EL >> 85% Saline
   Solubility: 10 mg/mL (27.07 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: 0.25 mg/mL (0.68 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

HI-TOPK-032 is a potent and specific TOPK inhibitor.

In Vitro

HI-TOPK-032 strongly suppresses TOPK kinase activity but has little effect on extracellular signal-regulated kinase 1 (ERK1), c-jun-NH2-kinase 1, or p38 kinase activities. HI-TOPK-032 occupies the ATP-binding site of TOPK and fits the binding site very well. The compound forms hydrogen bonds with GLY83 and ASP151 and has a hydrophobic interaction with LYS30. However, HI-TOPK-032 at the highest concentration (5 μM) also inhibits MEK1 activity by 40%. HI-TOPK-032 also inhibits anchorage-dependent and -independent colon cancer cell growth by reducing ERK-RSK phosphorylation as well as increasing colon cancer cell apoptosis through regulation of the abundance of p53, cleaved caspase-7, and cleaved PARP[1].

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

In Vivo	Treatment of mice with 1 or 10 mg/kg of HI-TOPK-032 significantly inhibits HCT-116 tumor growth by more than 60% relative to the vehicle-treated group. Mice are well tolerated with HI-TOPK-032 treatment. The expression of p53 is strongly induced, and phosphorylation of ERK and RSK, a direct downstream protein of ERK, is markedly inhibited in the HI-TOPK-032-treated group[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	The effect of HI-TOPK-032 on ERK1, JNK1, and p38 activity is assessed by an in vitro kinase assay using ERK1 (active, 500 ng), inactive RSK2 (ERK1 substrate, 1 μg), JNK1 (active, 50 ng), c-Jun (JNK1 substrate, 1 μg) and p38 (active, 200 ng), and ATF2 (p38 substrate, 500 ng) with [γ-^{32}P]ATP. Briefly, the reaction is carried out in the presence of 10 μCi of [γ-^{32}P]ATP with HI-TOPK-032 (0.5, 1, 2, 5 μM) in 40 μL of reaction buffer. After incubation at room temperature for 30 minutes, the reaction is stopped by adding 10 μL protein loading buffer and the mixture is separated by SDS-PAGE[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [1]	HCT-116 colon cancer cells are treated with different doses of HI-TOPK-032 (1, 2, 5 μM). After incubation for 1, 2, or 3 days, 20 μL of CellTiter96 AQueous One Solution is added and then cells are incubated for 1 hour at 37°C in a 5% CO_2 incubator. Absorbance is measured at 492 nm[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice: Mice are divided into 4 groups: (i) untreated vehicle group; (ii) 1 mg HI-TOPK-032/kg of body weight; (iii) 10 mg HI-TOPK-032/kg of body weight; and (iv) no cells and 10 mg HI-TOPK-032/kg of body weight. HCT-116 cells are suspended in serum-free McCoy 5A medium and inoculated s.c. into the right flank of each mouse. HI-TOPK-032 or vehicle is injected 3 times per week for 25 days. Tumor volume is calculated[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Oncol Rep. 2022 Jul;48(1):125.

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REFERENCES

[1]. Kim DJ, et al. Novel TOPK inhibitor HI-TOPK-032 effectively suppresses colon cancer growth. Cancer Res. 2012 Jun 15;72(12):3060-8.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA