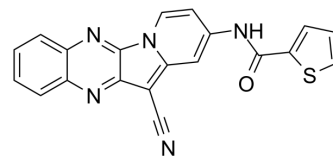


HI-TOPK-032

| | |
|--------------------|--|
| Cat. No.: | HY-101550 |
| CAS No.: | 487020-03-1 |
| Molecular Formula: | C ₂₀ H ₁₁ N ₅ OS |
| 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 | <div><div>Solvent</div><div>Concentration</div></div> | Mass | 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 | <p>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.</p> |

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 -³²P]ATP. Briefly, the reaction is carried out in the presence of 10 µCi of [γ -³²P]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% CO₂ 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.

Caution: Product has not been fully validated for medical applications. For research use only.

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