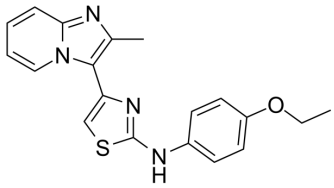
JK184

Cat. No.:	HY-13307
CAS No.:	315703-52-7
Molecular Formula:	$C_{19}H_{18}N_4OS$
Molecular Weight:	350.44
Target:	Hedgehog
Pathway:	Stem Cell/Wnt
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 : ≥ 50 mg/mL (142.68 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.8536 mL	14.2678 mL	28.5356 mL
	5 mM	0.5707 mL	2.8536 mL	5.7071 mL
	10 mM	0.2854 mL	1.4268 mL	2.8536 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 (7.13 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (7.13 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (7.13 mM); Clear solution

BIOLOGICAL ACTIVITY

Description	JK184 is a potent Hedgehog (Hh) pathway inhibitor with IC_{50} of 30 nM in mammalian cells.
IC_{50} & Target	IC50: 30 nM (Hedgehog)[1]
In Vitro	JK184 is designed to antagonize Hh signaling by inhibiting glioma (Gli)-dependent transcriptional activity in a dose dependent manner. JK184 significantly inhibitts proliferation of HUVECs with IC_{50} of 6.3 μg/mL after three days incubation.

	To evaluate anti-tumor effect of JK184, MTT assay is conducted in Panc-1 and BxPC-3 cells after administration with indicated concentrations of compounds, half maximal inhibitory concentration (IC_{50}) of JK184 (23.7 ng/mL in anc-1 and 34.3 ng/mL in BxPC-3)[1]. Claudin-low cell lines are more sensitive to JK184 treatment than are MCF10a, MTSV1-7, or HMLE-shGFP and HMLE-pBP cells, and JK184 induced a dose-dependent decrease in glioma-associated oncogene homolog 1 (GLI1) transcript and protein levels in these cells. Treatment with the IC_{50} dose of JK184 enhances the proportion of HMLE-shEcad cells that stained with Annexin-V, but are negative for propidium iodide (PI) ($P<0.0001$, t test)[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	JK184 (5 mg/kg, injected intravenously) exhibits good anti-proliferative activity in subcutaneous Panc-1 and BxPC-3 tumor models, and is a good candidate as antitumor drug targeted Hh signaling. However, JK184 has a poor pharmacokinetic profile and bioavailability[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	The Shh-LIGHT2 cells are seeded in 96-well plates and grown to confluency. The Shh-LIGHT2 cells are treated with various concentrations of JK184 micelles or free JK184 or micelles in DMEM containing 0.5% CS, 0.1 mg/mL streptomycin, 100 U/mL penicillin, 5% Shh-N conditioned medium obtained from Shh-N-producing HEK293 cells. The treated cells are cultured further for 60 h, and firefly and Renilla luciferase activities are measured using a dual luciferase kit. Proliferation assay or apoptosis evaluation of HUVECs is measured using MTT method or FCM analysis, respectively. HUVECs are treated with a series concentration of free JK184, JK184 micelles, or blank MPEG-PCL micelles for 48 h, respectively. The mean percentage of cell inhibition or apoptosis is calculated[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice[1] Five-week-old female athymic (nu/nu) mice are used. BxPC-3 and Panc-1 tumors are established by s.c. injection of 1×10^7 cells. Mice bearing tumors around 100 mm^3 are selected and randomized into treatment groups (5 mice per group). Mice are injected intravenously every day for 30 days with 100 μL of NS (control), blank micelles, free JK184 (5 mg/kg body weight), or JK184 micelles (5 mg/kg body weight), respectively. Tumor length and width are determined every 3 days and tumor volume (TV) is calculated using the following formula: $TV=0.5\times length\times width^2$. At the end of experiment, mice are sacrificed. Solid tumors are removed and processed for immunohistochemical analysis and terminal deoxynucleotidyl transferase-mediated dUTP nick end labeling (TUNEL) assay. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Aging (Albany NY). 2020 Jul 20;12(16):16270-16293.
- J Oncol. 2020 Jun 2;2020:1657896.

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REFERENCES

[1]. Zhang N, et al. Biodegradable polymeric micelles encapsulated JK184 suppress tumor growth through inhibiting Hedgehog signaling pathway. Nanoscale. 2015 Feb 14;7(6):2609-24.

[2]. Colavito SA, et al. Significance of glioma-associated oncogene homolog 1 (GLI1) expression in claudin-low breast cancer and crosstalk with the nuclear factor kappa-light-chain-enhancer of activated B cells (NFκB) pathway. Breast Cancer Res. 2014 Sep 25;16

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

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