JIB-04

Cat. No.: HY-13953

CAS No.: 199596-05-9

Molecular Formula: $C_{17}H_{13}ClN_4$

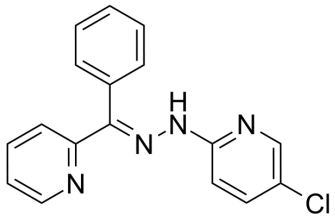
Molecular Weight: 308.76

Target: Histone Demethylase; Apoptosis

Pathway: Epigenetics; 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 : 50 mg/mL (161.94 mM; Need ultrasonic)
Ethanol : 2 mg/mL (6.48 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	3.2388 mL	16.1938 mL	32.3876 mL
5 mM	0.6478 mL	3.2388 mL	6.4775 mL
10 mM	0.3239 mL	1.6194 mL	3.2388 mL

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

In Vivo

1. Add each solvent one by one: 0.5% CMC-Na/saline water
   Solubility: 10 mg/mL (32.39 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (6.74 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.25 mg/mL (4.05 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

JIB-04 is a pan-selective Jumonji histone demethylase inihibitor with IC_{50}s of 230, 340, 855, 445, 435, 1100, and 290 nM for JARID1A, JMJD2E, JMJD3, JMJD2A, JMJD2B, JMJD2C, and JMJD2D, respectively.

IC_{50} & Target

IC50: 230 nM (JARID1A), 445 nM (JMJD2A), 435 nM (JMJD2B), 1100 nM (JMJD2C), 290 nM (JMJD2D), 340 nM (JMJD2E), 855 nM (JMJD3)[1]

In Vitro	JIB-04 is consistently selective for cancer vs. normal cells, demonstrated by the higher sensitivity of lung and prostate cancer lines (with IC_{50} as low as 10 nM) compared to HBECs and PrSCs/PrECs. JIB-04 inhibits cellular Jumonji demethylase activity, and Jumonji levels affect JIB-04 action in cells[1]. JIB-04 significantly inhibits the proliferation of GB cell lines and stem-enriched cultures. JIB-04 exerts its maximal inhibitory activity against KDM5A, and modulates the expression of genes involved in the control of cancer cell growth and leads to hypermethylation of H3K4. Furthermore, JIB-04 (2500 nM) activates the autophagy and apoptotic pathways and inactivates PI3K. JIB-04 also cooperates with TMZ in killing GB cells[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	JIB-04 results in a significant reduction in cancer-induced death rates in mice, prolonging survival[1]. JIB-04 (60, 40 and 20 mg/kg, i.p.) reaches bioactive concentration in the brain of the mice. The orthotopic GB xenograft model shows a trend toward longer survival in JIB-04-treated mice with an Hazard Ratio of 0.5[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	For cell viability assays, cells are plated at 1500-3000 cells/well in 96 well plates and treated the next day with increasing doses of compound over 4 days and their viability assessed by standard MTS assays using Promega's Cell Titer or Cell Titer-Glo reagents. Absorbance at 490 nm and 650 nm or luminescence is measured by a Spectra Max or a FlouroStar Omega plate reader. Data are normalized to the untreated controls (100% viability). Each cell line is tested in 2-5 independent assays, each containing 4-8 replicates. IC_{50} values are calculated using DIVISA, a high-throughput software, developed in house, for storing and analyzing drug sensitivity assays. Dose-response curves are plotted using a non-linear regression model and IC_{50}s are determined from the fitted curves. The average IC_{50} derived from 2-5 independent assays, each containing 4-8 replicates is reported. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	For xenografts, 4-6 week old female nude mice are housed under standard conditions in a clean facility at UTSW. Two million H358 cells or five million A549 cells are injected subcutaneously and allowed to grow for 2-3 weeks with monitoring. When tumors reach appr 200 mm^3, therapy is started in weight and tumor volume matched pairs (n=7 for each treatment group for each cell line). Drug or vehicle is administered by inter-peritoneal injection in 10% DMSO 90% sesame oil 2 to 3 times weekly for 5 weeks at 110 mg/kg to all mice harboring H358 xenografts or 3 times per week by gavage in 12.5% Cremophor EL, 12.5% DMSO as an aqueous suspension at 55 mg/kg to mice harboring A549 xenografts. Tumor volumes are monitored twice weekly by caliper measurements. Animals are weighed and observed during the five weeks of treatment. At the end point, mice are euthanized by CO_2 asphyxiation and cervical dislocation, and blood, tumors and major organs collected and weighed. Paired, unequal variance, one-tailed t-tests are performed across treatment groups using Excel software. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cancer Cell. 2019 Apr 15;35(4):677-691.e10.
- Proc Natl Acad Sci U S A. 2019 Feb 19;116(8):2961-2966.
- ACS Med Chem Lett. 2015 Jun 22;6(8):948-52.
- Exp Cell Res. 2021 Aug 2;112762.
- J Recept Signal Transduct Res. 2020 Aug;40(4):339-347.

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REFERENCES

[1]. Wang L, et al. A small molecule modulates Jumonji histone demethylase activity and selectively inhibits cancer growth. Nat Commun, 2013. 4: p. 2035.

[2]. Banelli B, et al. Small molecules targeting histone demethylase genes (KDMs) inhibit growth of temozolomide-resistant glioblastoma cells. Oncotarget. 2017 Apr 4.

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