

产品名称: JIB-04

产品别名: JIB-04

生物活性:					
Description	JIB-04 is a pan-selective Jumonji histone demethylase inhibitor 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 IC50 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].				
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].				
Solvent&Solubility	In Vitro: DMSO : 22.5 mg/mL (72.87 mM; Need ultrasonic and warming)				
	Preparing Stock Solutions	<div>Solvent / Mass / Concentration</div>	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
	*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液; 一旦配成溶液, 请分装保存, 避免反复冻融造成的产品失效。 储备液的保存方式和期限 -80°C, 6 months; -20°C, 1 month。 -80°C 储存时, 请在 6 个月内使用, -20°C 储存时, 请在 1 个月内使用。				
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.				
实验参考:					
Cell Assay	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 FlouoroStar 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. IC50 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 IC50s are determined from the fitted curves. The average IC50 derived from 2-5 independent assays, each containing 4-8 replicates is reported. [1]
Animal Administration	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. [1]
References	<p>[1]. Wang L, et al. A small molecule modulates Jumonji histone demethylase activity and selectively inhibits cancer growth. <i>Nat Commun</i>. 2013. 4: p. 2035.</p> <p>[2]. Banelli B, et al. Small molecules targeting histone demethylase genes (KDMs) inhibit growth of temozolomide-resistant glioblastoma cells. <i>Oncotarget</i>. 2017 Apr 4.</p>

源叶生物