产品名称：UMI-77
产品别名：UMI-77

生物活性：

Description

UMI-77 is a selective Mcl-1 inhibitor, which shows high binding affinity to Mcl-1 (IC_{50}=0.31 μM). UMI-77 binds to the BH3 binding groove of Mcl-1 with K_i of 490 nM, showing selectivity over other members of anti-apoptotic Bcl-2 members.

IC_{50} & Target [1]

Mcl-1	Bfl-1	Bcl-W	Bcl-2	Bcl-xL
0.49 μM (Ki)	5.33 μM (Ki)	8.19 μM (Ki)	23.83 μM (Ki)	32.99 μM (Ki)

In Vitro

Competitive binding curve of UMI-77 against Mcl-1 is obtained by FP based binding assay using fluorescent labeled Bid BH3 peptide with an IC50 of 1.87±0.22 μM. UMI-77 potently inhibits the cell growth of BxPC-3 and Panc-1 cell lines with IC50 values of 3.4 μM and 4.4 μM respectively, and shows 3 to 5 times less potency in inhibition of the cell growth of two other tested cell lines MiaPaCa-2 (12.5 μM) and AsPC-1 (16.1 μM). The cell growth inhibition potency of UMI-77 correlates with the highest expression of Mcl-1 and Bak, and lowest expression of Bcl-xL in the sensitive cell lines, BxPC-3 and Panc-1. Capan-2 cells are showing similar sensitivity to UMI-77 (IC50 of 5.5 μM) as BxPC-3 and Panc-1, although has low Mcl-1 levels[1].

In Vivo

UMI-77 exhibits moderate metabolic stability with a half-life of 45 minutes.The maximum tolerated dose (MTD) of UMI-77 in SCID mice is determined. Administered 60 mg/kg i.v. for 5 consecutive days per week for two weeks does not cause any loss in the animal weight and there is no obvious sign of toxicity during the course of the treatment. Increasing the dose to 80 mg/kg show severe animal weight loss (>20%), therefore 60 mg/kg is used as a therapeutic dose for the in vivo efficacy studies. Daily treatment with UMI-77 for 5 consecutive days a week for two weeks results in statistically significant tumor growth inhibition by 65% and 56% in comparison with the controls in day 19 (p<0.0001) and day 22 (p<0.003) respectively[1].

Solvent&Solubility

In Vitro:

DMSO : ≥ 28 mg/mL (59.79 mM)

H_2O : < 0.1 mg/mL (insoluble)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1352 mL	10.6760 mL	21.3520 mL
	5 mM	0.4270 mL	2.1352 mL	4.2704 mL
	10 mM	0.2135 mL	1.0676 mL	2.1352 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。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 **In Vitro** 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

	1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline Solubility: ≥ 2.5 mg/mL (5.34 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.34 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: 2.5 mg/mL (5.34 mM); Suspended solution; Need ultrasonic 此方案可获得 2.5 mg/mL (5.34 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。
References	[1]. Abulwerdi F, et al. A novel small-molecule inhibitor of mcl-1 blocks pancreatic cancer growth in vitro and in vivo. Mol Cancer Ther. 2014 Mar;13(3):565-575.

实验参考：

Cell Assay	Human PC cell lines AsPC-1, BxPC-3 and Capan-2 are cultured in RPMI 1640 medium, while Panc-1 and MiaPaCa are cultured in DMEM medium, all supplemented with 10% fetal bovine serum. The cell growth inhibition after treatment with increasing concentrations of the compounds (e.g., UMI-77; 1,10, and 100 μM) is determined by WST-8 assay[1].
Animal Administration	Mice[1] For BxPC-3 subcutaneous model, 10×10^6 cells are subcutaneously injected into the flanks of 4-5 week old female severe combined immune deficient mice (ICR-SCID). Palpable tumors start to appear in 3-5 weeks. Tumors are measured twice weekly. To prevent any pain or discomfort, mice are euthanized and their tumors remove once they reach ~1800 mg burden. Tumors are then dissected into 50 mg pieces and re-transplanted into naïve ICR-SCID for serial propagation. Animals are treated with either vehicle or UMI-77 given i.v. (60 mg/kg) on day three post BxPC-3 transplantation for two weeks (5 days a week). Tumor weight is recorded throughout the treatment period. At the end of the treatment period, animals are euthanized and their tumors harvested for protein isolation and western blot analysis for apoptotic markers.
References	[1]. Abulwerdi F, et al. A novel small-molecule inhibitor of mcl-1 blocks pancreatic cancer growth in vitro and in vivo. Mol Cancer Ther. 2014 Mar;13(3):565-575.