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产品名称：MI-538
产品别名：MI-538

生物活性：

Description	MI-538 is an inhibitor of the interaction between menin and MLL fusion proteins with an IC_{50} of 21 nM.
IC_{50} & Target	IC50 : 21 nM (menin and MLL interaction); Kd: 6.5 nM (menin)[1]
In Vitro	MI-538 inhibits the proliferation of MLL leukemia cells with a GI_{50} of 83 nM. MI-538 shows no effect (up to 6 μM) on growth of the control cell lines HL-60 and HM-2, which do not harbor MLL translocations, demonstrating good selectivity toward MLL fusion protein transformed cells. MI-538 binds to menin with low nanomolar affinity (K_d=6.5 nM). Its potent cellular activity originates from the improved binding affinity to menin and possibly increased cell membrane permeability. Treatment with MI-538 results in strong down regulation of expression of Hoxa9 and Meis1 genes. About 100 nM 27 was sufficient to reduce by ~50% Hoxa9 expression in MLL-AF9 cells, and even more pronounced effect was seen on Meis1 expression[1].
In Vivo	Treatment with MI-538 results in a pronounced, about 80%, reduction in the MV4;11 tumor volume, without causing substantial signs of toxicity reflected by less than 10% reduction of the body weight. MI-538 demonstrates markedly improved exposure (area under the curve, AUC, values), Cmax (maximum compound concentration) in the blood plasma, and the lowest value of clearance. The half-life of MI-538 is about 1.6 h. MI-538 has also high oral bioavailability (~50%)[1].

Solvent&Solubility

In Vitro:

DMSO : 100 mg/mL (**176.49 mM;** Need ultrasonic)

H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7649 mL	8.8246 mL	17.6491 mL
	5 mM	0.3530 mL	1.7649 mL	3.5298 mL
	10 mM	0.1765 mL	0.8825 mL	1.7649 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: ≥ 10 mg/mL (17.65 mM); Clear solution

此方案可获得 ≥ 10 mg/mL (17.65 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 100.0 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: 2.08 mg/mL (3.67 mM); Suspended solution; Need ultrasonic 此方案可获得 2.08 mg/mL (3.67 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 20.8 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。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 10 mg/mL (17.65 mM); Clear solution 此方案可获得 ≥ 10 mg/mL (17.65 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 100.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Borkin D, et al. Property Focused Structure-Based Optimization of Small Molecule Inhibitors of the Protein-Protein Interaction between Menin and Mixed Lineage Leukemia (MLL). J Med Chem. 2016 Feb 11;59(3):892-913.

实验参考：

Cell Assay	MOLM-13, MV4;11, HL-60 human leukemia cells as well as MLL-AF9 and HM-2 murine bone marrow cells are treated with MI-538 or 0.25% DMSO for 7 days. Media are changed at day 4 with viable cell number restored to the original concentration, and MI-538 are resupplied. An amount of 100 μL of cell suspension is transferred to 96-well plates for each sample in quadruplicates. Cell viability is measured using the MTT assay. Plates are read for absorbance at 570 nm[1].
Animal Administration	Mice: Mice xenograft are randomly grouped with each group containing eight mice. Vehicle or MI-538 (45 mg/kg) are administrated once daily at designated doses using ip injections for 2 weeks. Body weight and tumor sizes are monitored three times a week[1].
References	[1]. Borkin D, et al. Property Focused Structure-Based Optimization of Small Molecule Inhibitors of the Protein-Protein Interaction between Menin and Mixed Lineage Leukemia (MLL). J Med Chem. 2016 Feb 11;59(3):892-913.