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产品名称：TMP195
产品别名：TMP195

生物活性：

Description	TMP195 is a selective class IIa histone deacetylase (HDAC) inhibitor with an IC_{50} of 300 nM.

IC_{50} & Target	HDAC9	HDAC7	HDAC5	HDAC4	HDAC8	HDAC6
	9 nM (IC_{50})	46 nM (IC_{50})	106 nM (IC_{50})	111 nM (IC_{50})	11700 nM (IC_{50})	47800 nM (IC_{50})

In Vitro

TMP195 blocks the accumulation of CCL2 protein in the supernatants of monocyte-derived macrophage differentiation cultures. TMP195 significantly increases the amount of CCL1 protein secreted by the monocytes compared to vehicle group. In the transcriptional profiling data from the PHA-stimulated PBMC experiments, CCL2 and CCL1 are respectively down- or upregulated by TMP195[1]. TMP195 occupies the acetyllysine-binding site of class IIa HDACs. TMP195 competes against binding of HDAC7 to a variety of side-chain modifications on the same peptide backbone, despite no interference with the activity of other acetyllysine reader proteins BRD4 (IC50>50 μM)[2].

In Vivo

TMP195 treatment alters the tumour microenvironment and reduces tumour burden and pulmonary metastases by modulating macrophage phenotypes. TMP195 induces the recruitment and differentiation of highly phagocytic and stimulatory macrophages within tumors. Combining TMP195 with chemotherapy regimens or T-cell checkpoint blockade in this model significantly enhances the durability of tumour reduction[2].

Solvent&Solubility

In Vitro:

DMSO : ≥ 100 mg/mL (219.10 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	2.1910 mL	10.9548 mL	21.9096 mL
	5 mM	0.4382 mL	2.1910 mL	4.3819 mL
	10 mM	0.2191 mL	1.0955 mL	2.1910 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: ≥ 3 mg/mL (6.57 mM); Clear solution

此方案可获得 ≥ 3 mg/mL (6.57 mM，饱和度未知) 的澄清溶液。

	以 1 mL 工作液为例，取 100 μL 30.0 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: 3 mg/mL (6.57 mM); Suspended solution; Need ultrasonic 此方案可获得 3 mg/mL (6.57 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 30.0 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。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 3 mg/mL (6.57 mM); Clear solution 此方案可获得 ≥ 3 mg/mL (6.57 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 30.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Lobera M, et al. Selective class IIa histone deacetylase inhibition via a nonchelating zinc-binding group. Nat Chem Biol. 2013 May;9(5):319-25. [2]. Guerriero JL, et al. Class IIa HDAC inhibition reduces breast tumors and metastases through anti-tumor macrophages. Nature. 2017 Mar 16;543(7645):428-432.

实验参考：

Animal Administration	Mice: For all mouse experiments, mice are treated with intraperitoneal (i.p.) injections of 50 μL of the vehicle dimethyl sulfoxide (DMSO) or 50 μL of TMP195 dissolved in 100% DMSO at a final concentration of 50 mg per kg daily[2].
Kinase Assay	Recombinant HDAC7 catalytic domain (amino acids 483-903) is labeled with DyLight 650 and applied to an arrayed library of 3,868 immobilized 20-mer peptides. Arrays are conducted using an automated TECAN HS4 microarray processing station, initiated by incubation with blocking buffer for 30 min at 30°C followed by ishing with saline containing 50 mM Tris Base and 0.1% Tween-20 (pH 7.2) before incubation with the labeled HDAC7 protein for 120 min at 4°C. In the case of TMP195 competition experiments, the labeled protein is pre-incubated with TMP195 for 30 min before application to the array. The microarrays are then ished before being dried and imaged with an scanner[2].
References	[1]. Lobera M, et al. Selective class IIa histone deacetylase inhibition via a nonchelating zinc-binding group. Nat Chem Biol. 2013 May;9(5):319-25. [2]. Guerriero JL, et al. Class IIa HDAC inhibition reduces breast tumors and metastases through anti-tumor macrophages. Nature. 2017 Mar 16;543(7645):428-432.