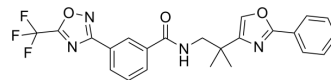


TMP195

Cat. No.:	HY-18361		
CAS No.:	1314891-22-9		
Molecular Formula:	C ₂₃ H ₁₉ F ₃ N ₄ O ₃		
Molecular Weight:	456.42		
Target:	HDAC		
Pathway:	Cell Cycle/DNA Damage; Epigenetics		
Storage:	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	2 years
		-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro	DMSO : 100 mg/mL (219.10 mM; Need ultrasonic)				
		Solvent Concentration	Mass 1 mg	5 mg	10 mg
	Preparing Stock Solutions	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	
Please refer to the solubility information to select the appropriate solvent.					
In Vivo	1. Add each solvent one by one: 15% Cremophor EL >> 85% Saline Solubility: 8.33 mg/mL (18.25 mM); Suspended solution; Need ultrasonic				
	2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline Solubility: ≥ 3 mg/mL (6.57 mM); Clear solution				
	3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline) Solubility: 3 mg/mL (6.57 mM); Suspended solution; Need ultrasonic				
	4. Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: ≥ 3 mg/mL (6.57 mM); Clear solution				

BIOLOGICAL ACTIVITY

Description	TMP195 is a selective class IIa histone deacetylase (HDAC) inhibitor with K _s of 59, 60, 26, 15 nM for HDAC4, HDAC5, HDAC7 and HDAC9, respectively.			
IC ₅₀ & Target	HDAC9 9 nM (IC ₅₀)	HDAC7 46 nM (IC ₅₀)	HDAC5 106 nM (IC ₅₀)	HDAC4 111 nM (IC ₅₀)

	HDAC8 11700 nM (IC ₅₀)	HDAC6 47800 nM (IC ₅₀)
In Vitro	<p>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].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>	
In Vivo	<p>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].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>	

PROTOCOL

Kinase Assay ^[2]	<p>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 washing 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 washed before being dried and imaged with a scanner^[2].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>
Animal Administration ^[2]	<p>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].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>

CUSTOMER VALIDATION

- Cancer Cell. 2021 Sep 1;S1535-6108(21)00445-1.
- Nat Biomed Eng. 2018 Aug;2(8):578-588.
- Nucleic Acids Res. 2022 Feb 12;gkac081.
- ACS Appl Mater Interfaces. 2023 Feb 14.
- Cell Death Dis. 2023 Feb 13;14(2):117.

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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.

Caution: Product has not been fully validated for medical applications. For research use only.

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