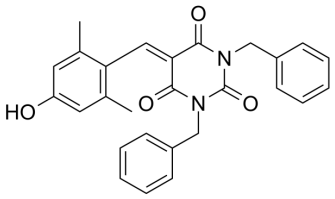
EML 425

Cat. No.:	HY-110263
CAS No.:	1675821-32-5
Molecular Formula:	$C_{27}H_{24}N_2O_4$
Molecular Weight:	440.49
Target:	Histone Acetyltransferase; Epigenetic Reader Domain
Pathway:	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 : ≥ 250 mg/mL (567.55 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.2702 mL	11.3510 mL	22.7020 mL
5 mM	0.4540 mL	2.2702 mL	4.5404 mL
10 mM	0.2270 mL	1.1351 mL	2.2702 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (4.72 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

EML425 is a potent and selective CREB binding protein (CBP)/p300 inhibitor with IC_{50}s of 2.9 and 1.1 μM, respectively.

IC_{50} & Target

IC50: 1.1 μM (p300), 2.9 μM (CBP)[1]

In Vitro

EML 425 (EML425, Compound 7h) is a potent and selective reversible inhibitor of CBP/p300, noncompetitive versus both acetyl-CoA and a histone H3 peptide, and endows with good cell permeability. EML 425 inhibits both p300 and CBP (IC_{50} values of 2.9 and 1.1 μM, respectively) while being practically inactive against the enzymes general control non derepressible-5 (GCN5) and p300/CBP-associated factor (PCAF). EML 425 induces a marked and time-dependent reduction in the acetylation of lysine H4K5 and H3K9 in U937 cells. EML 425 is shown to be a reversible inhibitor, noncompetitive versus both acetyl-CoA and a histone H3 peptide, and able to bind both the free enzyme and the enzyme-substrate complex, even with unequal affinity constants. The best scoring docking poses suggest that the binding site for EML 425 is an alternative

pocket lying near the substrate lysine binding groove and close to the acetylation site[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]

To explore the mechanisms of p300 inhibition by EML 425, reactions are performed. Each assay containing 5 nM p300, 3 μM Acetyl CoA, and 50 nM biotinylated H3 (1-21) peptide in 10 μL of assay buffer (50 mM Tris-HCl, pH 8.0, 0.1 mM EDTA, 1 mM DTT, 0.01% Tween-20, 0.01% BSA, 330 nM TSA) is incubated at room temperature for 15 min in a White opaque OptiPlate-384. Reactions are stopped by adding garcinol (final concentration 50 μM) and antiacetyl histone H3 lysine 9 (H3K9Ac) acceptor beads (final concentration 20 μg/mL). After 60 min of incubation at room temperature, 20 μg/mL final concentration of Alpha Streptavidin Donor beads are added in subdued light and incubated in the dark for 30 min at room temperature. Signals are read in Alpha mode with a Enspire plate reader[1].

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Cell Assay [1]

For cell cycle analysis, 500 μL of U937 cells (2.5×10^5 cells/mL) are seeded in 24-well plastic plates and incubated with 100 μM EML 425 for 72 h. After this period of treatment, 500 μL of hypotonic buffer (33 mM sodium citrate, 0.1% Triton X-100, 50 μg/mL propidium iodide) is added to cell suspensions. Cells are analyzed with a FACScan flow cytometer and quantitative analysis of cell cycle distribution and hypodiploid nuclei is performed using ModFit LT Macintosh software. All the experiments are performed at least in triplicate[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Osteoarthritis Cartilage. 2023 Sep 15;S1063-4584(23)00918-4.
- Biol Direct. 2023 Jul 6;18(1):37.

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REFERENCES

[1]. Milite C, et al. A novel cell-permeable, selective, and noncompetitive inhibitor of KAT3 histone acetyltransferases from a combined molecular pruning/classical isosterism approach. J Med Chem. 2015 Mar 26;58(6):2779-98.

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