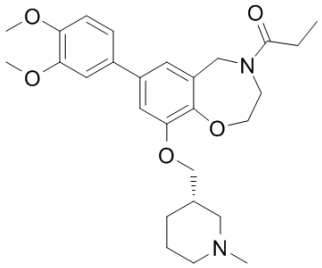
I-CBP112

Cat. No.:	HY-19541
CAS No.:	1640282-31-0
Molecular Formula:	$C_{27}H_{36}N_2O_5$
Molecular Weight:	468.59
Target:	Histone Acetyltransferase; Epigenetic Reader Domain
Pathway:	Epigenetics
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 32 mg/mL (68.29 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.1341 mL	10.6703 mL	21.3406 mL
5 mM	0.4268 mL	2.1341 mL	4.2681 mL
10 mM	0.2134 mL	1.0670 mL	2.1341 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: ≥ 2.5 mg/mL (5.34 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.34 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.34 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

I-CBP112 is a specific and potent acetyl-lysine competitive protein-protein interaction inhibitor, that inhibits the CBP/p300 bromodomains, enhances acetylation by p300.

IC_{50} & Target

IC50: 5.5±1.1 μM (CBP/p300, Leukemia cell); 9.1±1.2 μM (CBP/p300, Prostate cancer cell)[1]

In Vitro

I-CBP112 significantly enhances acetylation by p300 at the histone H3K18 and H3K23 sites. I-CBP112 stimulated H3K18ac by

	~3-fold, I-CBP112 induced enhances acetylation of these same sites by CBP as well as at H4K5. The EC_{50}'s of activation of I-CBP112 on p300- and CBP-mediated H3K18 acetylation are ~2 μM[1]. Exposure of human and mouse leukemic cell lines to I-CBP112 results in substantially impaired colony formation and induces cellular differentiation without significant cytotoxicity. Exposure of the BioMAP primary cell panel to I-CBP112 results in a unique response on cytokine and marker protein expression[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	I-CBP112 significantly reduces the leukemia-initiating potential of mLL-AF9+ AmL cells in a dose-dependent manner in vitro and in vivo. The synergistic effects of I-CBP112 and current standard therapy (doxorubicin) as well as emerging treatment strategies (BET inhibition) provide new opportunities for combinatorial treatment of leukemia and potentially other cancers [2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	I-CBP112 is dissolved in DMSO and diluted with appropriate medium before use. Cells (6000 KG1a and 13000 LNCaP cells/well) are plated in 96-well flat-bottom plates approximately 24 h prior to drug treatment. After 24 h, 10–20% fetal bovine serum-containing medium is replaced with 2.5% serum medium, and cells are treated with I-CBP112 in 0.18% DMSO; 0.18% DMSO is shown to have negligible cell growth effects under the conditions used in our experiments. After being exposed to I-CBP112 for 66 h, cells are subjected to a final concentration of 0.476% [3H]thymidine per well and allowed to proliferate for an additional 6 h (exposure to I-CBP112 for a total of 72 h). Cells are harvested, and the counts of 3H in each well are taken relative to those treated with vehicle alone to quantify the effect of the ligand on proliferation[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	Mice: Leukemic blasts expressing MLL-AF9 are treated in liquid culture with 5 μM of I-CBP112 for 3 days. Control cells are exposed to the corresponding concentration of the DMSO vehicle. Treated cells are then transplanted into sublethally irradiated syngeneic mice via tail vein injection. Upon the development of signs of disease the mice are sacrificed and analysed[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Res. 2021 Mar;31(3):291-311.

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REFERENCES

[1]. Zucconi BE, et al. Modulation of p300/CBP Acetylation of Nucleosomes by Bromodomain LigandI-CBP112. Biochemistry. 2016 Jul 12;55(27):3727-34.

[2]. Picaud S, et al. Generation of a Selective Small Molecule Inhibitor of the CBP/p300 Bromodomain for Leukemia Therapy. Cancer Res. 2015 Dec 1;75(23):5106-19.

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

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA