

Product Data Sheet

Product Name: I-CBP112

Cat. No.: GC34078

Chemical Properties

Cas. No. 1640282-31-0

SMILES COC1=C(OC)C=C(C2=CC(OC[C@H]3CCCCN(C)C3)=C(OCCN(C(CC)=O)C4)C4=C2)C=C1

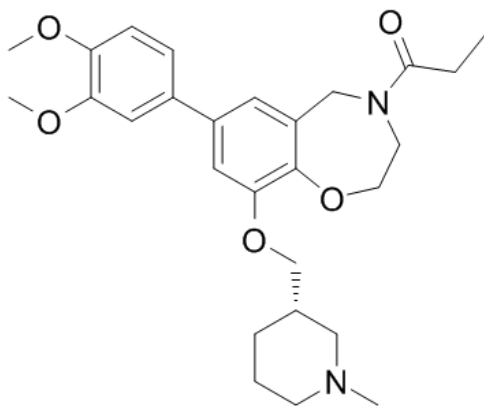
Formula $C_{27}H_{36}N_2O_5$ M.Wt 468.59

Solubility DMSO : ≥ 32 mg/mL (68.29 mM) Storage Store at -20°C

General tips For obtaining a higher solubility , please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.

Structure



Protocol

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

Cell experiment: 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].

Animal experiment: Mice: Leukemic blasts expressing MLL-AF9 are treated in liquid culture with 5 μ M 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].

References:

- [1]. Zucconi BE, et al. Modulation of p300/CBP Acetylation of Nucleosomes by Bromodomain Ligand I-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.

Background

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

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

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

sites by CBP as well as at H4K5. The EC₅₀'s of activation of I-CBP112 on p300- and CBP-mediated H3K18 acetylation are ~2 μ M[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].

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].

[1]. Zucconi BE, et al. Modulation of p300/CBP Acetylation of Nucleosomes by Bromodomain Ligand I-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: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA