产品名称：4-[4-[[5-(4,5-二甲基-2-硝基苯基)-2-呋喃基]亚甲基]-4,5-二氢-3-甲基-5-氧代-1H-吡唑-1-基]-苯甲酸
产品别名：C646

生物活性：

Description	C646 is a selective and competitive histone acetyltransferase p300 inhibitor with K_i of 400 nM, and is less potent for other acetyltransferases.
IC_{50} & Target	Ki: 400 nM (histone acetyltransferase p300)
In Vitro	C646 is a linear competitive inhibitor of p300 versus acetyl-CoA with a Ki of 400 nM. C646 shows a noncompetitive pattern of p300 inhibition versus H4-15 peptide substrate. C646 treatment reduces histone H3 and H4 acetylation levels and abrogates TSA-induced acetylation in cells. C646 has a more potent effect on cell growth than Lys-CoA-Tat does[1]. C646 enhances mitotic catastrophe after IR and suppresses phosphorylation of CHK1 after IRin A549 cells[2]. C646 attenuates the increased acetylation of GATA1 and the increased transcriptional activity of GATA1 induced by EDAG[3].
Solvent&Solubility	***In Vitro:*** **DMSO : ≥ 36 mg/mL (80.82 mM)** * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2451 mL	11.2254 mL	22.4507 mL
	5 mM	0.4490 mL	2.2451 mL	4.4901 mL
	10 mM	0.2245 mL	1.1225 mL	2.2451 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。

References

[1]. Bowers EM, et al. Virtual ligand screening of the p300/CBP histone acetyltransferase: identification of a selective small molecule inhibitor. Chem Biol. 2010 May 28;17(5):471-82.

[2]. Oike T, et al. C646, a selective small molecule inhibitor of histone acetyltransferase p300, radiosensitizes lung cancer cells by enhancing mitotic catastrophe. Radiother Oncol. 2014 May;111(2):222-7.

[3]. Zheng WW, et al. EDAG positively regulates erythroid differentiation and modifies GATA1 acetylation through recruiting p300. Stem Cells. 2014 Aug;32(8):2278-89.

实验参考：

Cell Assay	Cells are seeded in 6-well plates, incubated at 37°C for 4-10 h for attachment, and exposed (or not) to C646. After incubation for 2 h, the cells are subjected (or not) to IR and incubated for 10 days for colony formation. The cells are fixed with methanol and stained with crystal violet. Colonies of at least 50 cells are counted. The surviving fraction is normalized to the corresponding controls. The dose required to reduce the surviving fraction to 10% (D10) of the irradiated cells is calculated by using the linear-quadratic model. [2]
	Reactions are carried out at 30°C for times varying from 2 to 4 min under the following reaction conditions: 50 mM HEPES, pH 7.9, 50 mM NaCl, 0.05 mg/mL BSA, 5 mM DTT, 0.05 mM EDTA,

Kinase Assay	0.25% DMSO, 10 μM of X. laevis histone H3, and varying concentrations of C646 (0, 3, 10 μM). The reactions contains either 70 nanograms of Rtt109/Vps75, 15 nanograms of yGcn5, 300 nanograms of the SAS complex or 1 microgram of hMOZ. The amount of enzyme used in each assay is estimated by comparing Coomassie Blue staining of samples with bovine serum albumin standards, analyzed by SDS-PAGE. The mixture is allowed to equilibrate at 30°C for 10 min before the reaction is initialed with addition of a 1:1 mixture of ^{12}C-AcCoA and ^{14}C-AcCoA to a final concentration of 20 μM. After the appropriate time the reaction is quenched with 6 X Tris-Tricine gel loading buffer which contains 0.2mol/LTris-Cl pH 6.8, 40% v/v glycerol, 14% w/v SDS, 0.3 mol/LDTT, and 0.06% w/v Coomassie Blue. The ^{14}C-labeled histone substrates are separated from reactants on a 16.5% Tris-Tricine SDS-PAGE gel. The rate of ^{14}C-incorporation into histone H3 is quantified by autoradiography. All assays are in duplicate, and these generally agree within 20%.[1]
References	[1]. Bowers EM, et al. Virtual ligand screening of the p300/CBP histone acetyltransferase: identification of a selective small molecule inhibitor. Chem Biol. 2010 May 28;17(5):471-82. [2]. Oike T, et al. C646, a selective small molecule inhibitor of histone acetyltransferase p300, radiosensitizes lung cancer cells by enhancing mitotic catastrophe. Radiother Oncol. 2014 May;111(2):222-7. [3]. Zheng WW, et al. EDAG positively regulates erythroid differentiation and modifies GATA1 acetylation through recruiting p300. Stem Cells. 2014 Aug;32(8):2278-89.