Belinostat

Cat. No.: HY-10225

CAS No.: 866323-14-0

Molecular Formula: $C_{15}H_{14}N_2O_4S$

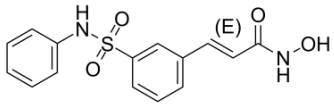
Molecular Weight: 318.35

Target: HDAC; Autophagy

Pathway: Cell Cycle/DNA Damage; Epigenetics; Autophagy

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 : ≥ 150 mg/mL (471.18 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	3.1412 mL	15.7060 mL	31.4120 mL
5 mM	0.6282 mL	3.1412 mL	6.2824 mL
10 mM	0.3141 mL	1.5706 mL	3.1412 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 (7.85 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (7.85 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (7.85 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Belinostat (PXD101; PX105684) is a potent HDAC inhibitor with an IC_{50} of 27 nM in HeLa cell extracts.

IC_{50} & Target

HDAC6	HDAC
82 nM (IC_{50})	27 nM (IC_{50}, Hela cell)

In Vitro

Belinostat (PXD101) induces a concentration-dependent (0.2-5 μM) increase in acetylation of histone H4 in tumor cell lines.

	Belinostat is cytotoxic in vitro in a number of tumor cell lines with IC_{50}s in the range 0.2-3.4 μM as determined by a clonogenic assay and induces apoptosis. Belinostat inhibits the growth of a number of human tumor cell lines in vitro with IC_{50}s determined by a clonogenic assay in the range 0.2-3.4 μM[1]. Belinostat (PXD101) is a potent histone deacetylase (HDAC) inhibitor, potently inhibits the enzymatic activity of purified recombinant HDAC6 (IC_{50} of 82 nM)[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Treatment of nude mice bearing human ovarian and colon tumor xenografts with Belinostat (10-40 mg/kg/day i.p.) daily for 7 days causes a significant dose-dependent growth delay with no obvious signs of toxicity to the mice. Growth delay is also observed for xenografts of cisplatin-resistant ovarian tumor cells. A marked increase in acetylation of H4 is detected in blood and tumor of mice 3 h after treatment with Belinostat (PXD101). The inhibition of growth of human tumor xenografts in mice, with no apparent toxicity[1]. Belinostat (PXD101) displays single-agent antitumor activity on human A2780 ovarian cancer s.c. xenografts which is enhanced via combination therapy with Carboplatin[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	For activity assays, the reaction is carried out in a total volume of 150 μL of buffer [60 mM Tris (pH 7.4) containing 30% glycerol] containing 2 μL of cell extract and, where used, 2 μL of Belinostat. The reaction is started by the addition of 2 μL of [^{3}H]labeled substrate (acetylated histone H4 peptide corresponding to the 20 NH_2-terminal residues). Samples are incubated at 37°C for 45 min, and the reaction stopped by the addition of HCl and acetic acid (0.72 and 0.12 M final concentrations, respectively). Released [^{3}H]acetate is extracted into 750 μL of ethyl acetate, and samples are centrifuged at 12,000× g for 5 min. The upper phase (600 μL) is transferred to 3 mL of scintillation fluid and counted[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [1]	The human ovarian cell line A2780 and Cisplatin (A2780/cp70) and Doxorubicin (2780AD) resistant derivatives are grown in RPMI 1640 supplemented with glutamine (2 mM) and FCS (10%). The human colon (HCT116 and HT29), melanoma (HS852), prostate (PC3), lung (CALU-3), and breast (MCF7) cell lines are grown in RPMI 1640 and the rest in DMEM supplemented as above. The human non-small cell lung cancer cell line WIL is grown in DMEM supplemented as above. Drug sensitivity is determined by a clonogenic assay. Briefly, cells are plated in 5 mL of medium at a density of 8×10^4 cells/25 cm^2 flask and allowed to attach and grow for 48 h. Cells are exposed to Belinostat (five concentrations from 0.016 to 10 μM) for 24 h. The medium is removed, and 1 mL of trypsin/EDTA is added to each flask. Once the cells have detached, 1 mL of medium is added, the cells are resuspended, and those from the control untreated flask are counted. Cells are diluted and plated into 6-cm Petri dishes (three per flask) at a density of 500-2000 cells/dish depending on the cell line. Cells from the drug-treated flasks are diluted and plated as for the control flasks. Dishes are incubated for 10-15 days at 37°C. Cells are washed with PBS, fixed in methanol, and stained with crystal violet, and colonies that contained ≥50 cells counted. Sensitivity is expressed as the IC_{50} (mean±SE of three experiments) defined as the concentration of drug required to reduce the number of colonies to 50% of that of the control untreated cells[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice[1] For the human tumor xenograft studies, monolayer cultures are harvested with trypsin/EDTA (0.25%/1 mM in PBS) and resuspended in PBS. About 10^7 cells are injected s.c. into the right flank of athymic nude mice (CD1 nu/nu mice). After 10-15 days when the mean tumor diameter is ≥0.5 cm, animals are randomized into groups of six for experiments. Belinostat is dissolved in DMSO and then diluted in water to give a final concentration of DMSO of 10% and is administered i.p. at the times specified. This formulation gives sufficient solubility for doses of ≤ 40 mg/kg. Mice are weighed daily, and tumor volumes are estimated by caliper measurements assuming spherical geometry (volume=$d^3\times\pi/6$). MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nat Commun. 2017 Sep 5;8(1):435.
- Cell Syst. 2018 Apr 25;6(4):424-443.e7.
- Cell Death Dis. 2019 May 24;10(6):400.
- Cell Death Dis. 2018 Jan 26;9(2):129.
- Viruses. 2020 Jun 3;12(6):E609.

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REFERENCES

[1]. Plumb JA, et al. Pharmacodynamic response and inhibition of growth of human tumor xenografts by the novel histonedeacetylase inhibitor PXD101. Mol Cancer Ther. 2003 Aug;2(8):721-8.

[2]. Qian X, et al. Activity of PXD101, a histone deacetylase inhibitor, in preclinical ovarian cancer studies. Mol Cancer Ther. 2006 Aug;5(8):2086-95.

[3]. Chia S, et al. Phenotype-driven precision oncology as a guide for clinical decisions one patient at a time. Nat Commun. 2017 Sep 5;8(1):435.

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