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产品名称: 贝利司他  
产品别名: **Belinostat ; PXD101; PX105684**

生物活性:

Description	Belinostat (PXD101; PX105684) is a potent HDAC inhibitor with an IC50 of 27 nM in HeLa cell extracts.				
IC50 & Target	HDAC6	HDAC			
	82 nM (IC50)	27 nM (IC50, 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 IC50s 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 IC50s 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 (IC50 of 82 nM)[2].				
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].				
Solvent&Solubility	<b>In Vitro:</b> <b>DMSO : ≥ 150 mg/mL (471.18 mM)</b>  * "≥" means soluble, but saturation unknown.				
	Preparing Stock Solutions	<div><div>Solvent</div><div>Mass</div><div>Concentration</div></div>	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
	*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℃, 6 months; -20℃, 1 month。 -80℃ 储存时, 请在 6 个月内使用, -20℃ 储存时, 请在 1 个月内使用。 <b>In Vivo:</b> 请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液, 再依次添加助溶剂:  ——为保证实验结果的可靠性, 澄清的储备液可以根据储存条件, 适当保存; 体内实验的工作液, 建议您现用现配, 当天使用; 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比; 如在配制过程中出现沉淀、析出现象, 可以通过加热和/或超声的方式助溶  1.请依序添加每种溶剂: 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline  Solubility: ≥ 2.5 mg/mL (7.85 mM); Clear solution  此方案可获得 ≥ 2.5 mg/mL (7.85 mM, 饱和度未知) 的澄清溶液。				



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	<p>以 1 mL 工作液为例, 取 100 <math>\mu</math>L 25.0 mg/mL 的澄清 DMSO 储备液加到 400 <math>\mu</math>L PEG300 中, 混合均匀向上述体系中加入 50 <math>\mu</math>L Tween-80, 混合均匀; 然后继续加入 450 <math>\mu</math>L 生理盐水定容至 1 mL。</p> <p>2. 请依序添加每种溶剂: 10% DMSO <math>\rightarrow</math> 90% (20% SBE-<math>\beta</math>-CD in saline)</p> <p>Solubility: <math>\geq</math> 2.5 mg/mL (7.85 mM); Clear solution</p> <p>此方案可获得 <math>\geq</math> 2.5 mg/mL (7.85 mM, 饱和度未知) 的澄清溶液。</p> <p>以 1 mL 工作液为例, 取 100 <math>\mu</math>L 25.0 mg/mL 的澄清 DMSO 储备液加到 900 <math>\mu</math>L 20% 的 SBE-<math>\beta</math>-CD 生理盐水水溶液中, 混合均匀。</p> <p>3. 请依序添加每种溶剂: 10% DMSO <math>\rightarrow</math> 90% corn oil</p> <p>Solubility: <math>\geq</math> 2.5 mg/mL (7.85 mM); Clear solution</p> <p>此方案可获得 <math>\geq</math> 2.5 mg/mL (7.85 mM, 饱和度未知) 的澄清溶液, 此方案不适用于实验周期在半个月以上的实验。</p> <p>以 1 mL 工作液为例, 取 100 <math>\mu</math>L 25.0 mg/mL 的澄清 DMSO 储备液加到 900 <math>\mu</math>L 玉米油中, 混合均匀。</p>
References	<p>[1]. Plumb JA, et al. Pharmacodynamic response and inhibition of growth of human tumor xenografts by the novel histone deacetylase inhibitor PXD101. Mol Cancer Ther. 2003 Aug;2(8):721-8.</p> <p>[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.</p> <p>[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.</p>
实验参考:	
Cell Assay	<p>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 <math>8 \times 10^4</math> cells/25 cm<sup>2</sup> flask and allowed to attach and grow for 48 h. Cells are exposed to Belinostat (five concentrations from 0.016 to 10 <math>\mu</math>M) 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 <math>\geq</math>50 cells counted. Sensitivity is expressed as the IC<sub>50</sub> (mean <math>\pm</math> 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].</p>
	<p>Mice[1]</p> <p>For the human tumor xenograft studies, monolayer cultures are harvested with trypsin/EDTA (0.25%/1 mM in PBS) and resuspended in PBS. About <math>10^7</math> cells are injected s.c. into the right flank</p>



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<b>Animal Administration</b>	of athymic nude mice (CD1 <i>nu/nu</i> mice). After 10-15 days when the mean tumor diameter is $\geq 0.5$ 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 $\leq 40$ mg/kg. Mice are weighed daily, and tumor volumes are estimated by caliper measurements assuming spherical geometry (volume= $d^3 \times \pi/6$ ).
<b>Kinase Assay</b>	For activity assays, the reaction is carried out in a total volume of 150 $\mu$ L of buffer [60 mM Tris (pH 7.4) containing 30% glycerol] containing 2 $\mu$ L of cell extract and, where used, 2 $\mu$ L of Belinostat. The reaction is started by the addition of 2 $\mu$ L of [ $^3$ H]labeled substrate (acetylated histone H4 peptide corresponding to the 20 NH <sub>2</sub> -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 $\mu$ L of ethyl acetate, and samples are centrifuged at 12,000 $\times$ g for 5 min. The upper phase (600 $\mu$ L) is transferred to 3 mL of scintillation fluid and counted[1].
<b>References</b>	<p>[1]. Plumb JA, et al. Pharmacodynamic response and inhibition of growth of human tumor xenografts by the novel histone deacetylase inhibitor PXD101. Mol Cancer Ther. 2003 Aug;2(8):721-8.</p> <p>[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.</p> <p>[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.</p>