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产品名称：NSC 663284
产品别名：DA-3003-1

生物活性：

Description	NSC 663284 is a potent, cell-permeable, and irreversible Cdc25 dual specificity phosphatase inhibitor, has an IC_{50} for Cdc25B2 of 0.21 μM. NSC 663284 exhibits mixed competitive kinetics against Cdc25A, Cdc25B(2), and Cdc25C with Ki values of 29, 95, and 89 nM, respectively[1]. NSC 663284 inhibits NSD2 (IC_{50} of 170 nM) through a direct interaction with the catalytic SET domain (K_d of 370 nM)[2].
IC_{50} & Target	IC50: 0.21 μM (Cdc25B2)[1]
In Vitro	NSC 663284 (3-100μM; 48 hours) has a mean IC_{50} value in the NCI 60 Cell human tumor panel of 1.5 ± 0.6 μM, has IC_{50} values of 0.2 μM in human breast cancer MDA-MB-435 and MDA-N cells, has an IC_{50} value of 1.7 μM in human breast MCF-7 cells in culture[1]. NSC 663284 has relative IC_{50} values for Cdc25B2 (IC_{50}=0.21 μM) are 20- and 450-fold lower than for VHR (IC_{50}=4.0 μM) or PTP1B (IC_{50}>4.0 μM), respectively[1].
In Vivo	NSC 663284 (intravenous injection; 2, 3, and 5mg/kg) inhibits the growth of subcutaneous human colon HT29 xenografts in SCID mice. After a single dose of 5 mg/kg, NSC 663284 is not detectable in plasma or tissues beyond 5 min. Following NSC 663284 treatment of tumor-bearing SCID mice, reduces glutathione concentrations in HT29 tumor are decreased to a greater extent and remained decreased for longer than the reduced glutathione concentrations in liver and kidneys[3].

Solvent&Solubility

In Vitro:

DMSO : ≥ 150 mg/mL (466.19 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.1079 mL	15.5395 mL	31.0791 mL
	5 mM	0.6216 mL	3.1079 mL	6.2158 mL
	10 mM	0.3108 mL	1.5540 mL	3.1079 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。

In Vivo:

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 (7.77 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (7.77 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；

	向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (7.77 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (7.77 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (7.77 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (7.77 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。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Lazo JS, et al. Discovery and biological evaluation of a new family of potent inhibitors of the dual specificity protein phosphatase Cdc25. J Med Chem. 2001 Nov 22;44(24):4042-9. [2]. Coussens NP, et al. High-throughput screening with nucleosome substrate identifies small-molecule inhibitors of the human histone lysine methyltransferase NSD2. J Biol Chem. 2018 Aug 31;293(35):13750-13765. [3]. Guo J, et al. Pharmacology and antitumor activity of a quinolinedione Cdc25 phosphatase inhibitor DA3003-1 (NSC 663284). Anticancer Res. 2007 Sep-Oct;27(5A):3067-73.

实验参考：

Animal Administration	Mice: C.B.-17 SCID mice bearing HT29 human colon carcinoma xenografts are stratified into the following groups of 9-10 animals: Control, vehicle control, positive control (gemcitabine, 50 mg/kg/dose i.v.), NSC 663284 at the following doses: 2, 3 or 5 mg/kg/dose i.v.. The mice are dosed every 4 days for 6 doses, and body weights and tumor volumes are recorded twice weekly. Tumors are measured with calipers, and tumor volumes are calculated. Mice are followed for 3 weeks following the completion of the dosing to monitor tumor regrowth. In a second study, C.B.-17 SCID mice bearing MDA-MB-435 human breast cancer xenografts are stratified to the same treatment groups, except that paclitaxel at 20 mg/kg i.v. every 7 days is used as the positive control[2].
References	[1]. Lazo JS, et al. Discovery and biological evaluation of a new family of potent inhibitors of the dual specificity protein phosphatase Cdc25. J Med Chem. 2001 Nov 22;44(24):4042-9. [2]. Coussens NP, et al. High-throughput screening with nucleosome substrate identifies small-molecule inhibitors of the human histone lysine methyltransferase NSD2. J Biol Chem. 2018 Aug 31;293(35):13750-13765. [3]. Guo J, et al. Pharmacology and antitumor activity of a quinolinedione Cdc25 phosphatase inhibitor DA3003-1 (NSC 663284). Anticancer Res. 2007 Sep-Oct;27(5A):3067-73.