产品名称：SB216763
产品别名：SB 216763

生物活性：

Description	SB 216763 is potent, selective and ATP-competitive GSK-3 inhibitor with IC_{50}s of 34.3 nM for both GSK-3α and GSK-3β.	
IC_{50} & Target	GSK-3α	GSK-3β
	34.3 nM (IC_{50})	34.3 nM (IC_{50})
In Vitro	SB-216763 (10-20 μM) induces β-catenin mediated-transcription in a dose-dependent manner in HEK293 cells. SB-216763 (10, 15 and 20 μM) can maintain mESCs with a pluripotent-like morphology in long-term culture. SB-216763 (10 μM) can maintain J1 mESCs in a pluripotent state for more than a month[2]. SB-216763 inhibits GSK-3 with IC50 of 34 nM[3]. SB-216763 is equally effective at inhibiting human GSK-3α and GSK-3β[5]..	
In Vivo	SB216763 (20 mg/kg, i.v.) significantly improves the survival of BLM-treated mice. Mice randomized to receive BLM plus SB216763 shows a noteworthy reduction, compared with BLM-treated mice. SB216763 (20 mg/kg, i.v.) reduces the magnitude of BLM-induced alveolitis[1]. SB 216763 (0.2 mg/kg, i.v.) with either 17β-E100 or Geni100 reverses the ceiling effect because these agents significantly reduce infarct size when the rabbits' hearts are submitted to 30-min CAO[4].	

Solvent&Solubility

In Vitro:

DMSO : 100 mg/mL (**269.38 mM**; Need ultrasonic)

H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.6938 mL	13.4691 mL	26.9382 mL
	5 mM	0.5388 mL	2.6938 mL	5.3876 mL
	10 mM	0.2694 mL	1.3469 mL	2.6938 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 (6.73 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (6.73 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 (6.73 mM); Suspended solution; Need ultrasonic 此方案可获得 2.5 mg/mL (6.73 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。 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 (6.73 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.73 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]. Gurrieri, et al. 3-(2,4-dichlorophenyl)-4-(1-methyl-1H-indol-3-yl)-1H-pyrrole-2,5-dione (SB216763), a glycogen synthase kinase-3 inhibitor, displays therapeutic properties in a mouse model of pulmonary inflammation and fibrosis. J.Pharmacol.Exp.Ther.2010 [2]. Kirby LA, et al. Glycogen synthase kinase 3 (GSK3) inhibitor, SB-216763, promotes pluripotency in mouse embryonic stem cells.PLoS One. 2012;7(6):e39329. Epub 2012 Jun 26. [3]. Wang M, et al. The first synthesis of [(11)C]SB-216763, a new potential PET agent for imaging of glycogen synthase kinase-3 (GSK-3).Bioorg Med Chem Lett. 2011 Jan 1;21(1):245-9. Epub 2010 Nov 11. [4]. The ceiling effect of pharmacological postconditioning with the phytoestrogen genistein is reversed by the GSK3beta inhibitor SB 216763 [3-(2,4-dichlorophenyl)-4(1-methyl-1H-indol-3-yl)-1H-pyrrole-2,5-dione] through mitochondrial ATP-dependent potassium channel opening. [5]. Coghlan MP, et al. Selective small molecule inhibitors of glycogen synthase kinase-3 modulate glycogen metabolism and gene transcription. Chem Biol. 2000 Oct;7(10):793-803. [6]. Wang W, et al. Inhibition of glycogen synthase kinase 3beta ameliorates triptolide-induced acute cardiac injury by desensitizing mitochondrial permeability transition. Toxicol Appl Pharmacol. 2016 Dec 15;313:195-203.

实验参考：

Cell Assay	MESCs maintained with LIF or 10 μM SB-216763 for more than a month are resuspended at 40,000 cells/mL in LIF-free mESC medium. EBs are prepared by a hanging drop procedure. Briefly, 20 μL drops containing mESCs are pipetted on the inside of a 10-cm Petri dish lid. The lids are placed onto Petri dishes containing 10 mL of HBSS and the EBs are allowed to form and grow for 4 days in the incubator. After 4 days, 15-20 EBs are transferred to a well containing LIF-free mESC medium in a 24-well plate. The medium is exchanged every two days and autonomously beating cell aggregates are observed and counted. [2]
Animal Administration	Mice are allocated to four groups (n=12/group) as follows: 1) intratracheal saline + vehicle (25% dimethyl sulfoxide, 25% polyethylene glycol, and 50% saline), 2) intratracheal saline + SB216763 (20 mg/kg) dissolved in vehicle, 3) intratracheal BLM (3 U/kg) + vehicle, and 4) intratracheal BLM + SB216763 (20 mg/kg) in vehicle. Another set of experiments to assess cytokine expression by reverse transcription-PCR is conducted in the mice (n=12/group) to receive 1) intratracheal saline + vehicle, 2) intratracheal BLM, and 3) intratracheal BLM + SB216763. To induce pulmonary fibrosis, BLM is intratracheally administered in mice (n=15/group) on day 0. BLM and saline-treated mice are administered with SB216763 dissolved in vehicle or vehicle alone intravenously at day 0 and then intraperitoneally twice a week until day 28. Mice are sacrificed by CO_2 inhalation on days 2, 7, and

	28. In the terminal deoxynucleotidyl transferase dUTP nick-end labeling (TUNEL) experiments, the cohorts of mice are as follows: saline-treated (n=6), BLM-treated (n=6), and BLM + SB216763-treated (n=6). [1]
References	[1]. Gurrieri, et al. 3-(2,4-dichlorophenyl)-4-(1-methyl-1H-indol-3-yl)-1H-pyrrole-2,5-dione (SB216763), a glycogen synthase kinase-3 inhibitor, displays therapeutic properties in a mouse model of pulmonary inflammation and fibrosis. J.Pharmacol.Exp.Ther.2010 [2]. Kirby LA, et al. Glycogen synthase kinase 3 (GSK3) inhibitor, SB-216763, promotes pluripotency in mouse embryonic stem cells.PLoS One. 2012;7(6):e39329. Epub 2012 Jun 26. [3]. Wang M, et al. The first synthesis of [(11)C]SB-216763, a new potential PET agent for imaging of glycogen synthase kinase-3 (GSK-3).Bioorg Med Chem Lett. 2011 Jan 1;21(1):245-9. Epub 2010 Nov 11. [4]. The ceiling effect of pharmacological postconditioning with the phytoestrogen genistein is reversed by the GSK3beta inhibitor SB 216763 [3-(2,4-dichlorophenyl)-4(1-methyl-1H-indol-3-yl)-1H-pyrrole-2,5-dione] through mitochondrial ATP-dependent potassium channel opening. [5]. Coghlan MP, et al. Selective small molecule inhibitors of glycogen synthase kinase-3 modulate glycogen metabolism and gene transcription. Chem Biol. 2000 Oct;7(10):793-803. [6]. Wang W, et al. Inhibition of glycogen synthase kinase 3beta ameliorates triptolide-induced acute cardiac injury by desensitizing mitochondrial permeability transition. Toxicol Appl Pharmacol. 2016 Dec 15;313:195-203.