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产品名称：SJG-136
产品别名：NSC-694501

生物活性：

Description	SJG-136 is a DNA cross-linking agent, with an XL50 of 45 nM for pBR322 DNA. SJG-136 has potent antitumor activity.
IC_{50} & Target	XL50: 45 nM (pBR322 DNA)[1]
In Vitro	SJG-136 (dimer 5) is a DNA cross-linking agent, with an XL50 (concentration of agent required for 50% cross-linking of pBR322 DNA) of 45 nM for pBR322 DNA. SJG-136 is cytotoxic to ovarian cell lines, such as A2780 (IC50, 22.5 pM), A2780cisR (IC50, 24 pM), CH1 (IC50, 0.12 nM), CH1cisR (IC50, 0.6 nM), and SKOV-3 (IC50, 9.1 nM)[1]. SJG-136 (SG2000) also reduces the viability of a panel of canine cancer cells, with GI50 values ranging from 0.33 - >100 nM after a 1 h exposure, and <0.03 - 17.33 nM following continuous exposure[2].
In Vivo	SJG-136 shows more potent antitumor effect against CMeC-1 tumour at 0.30 mg/kg than 0.15 mg/kg either as a single dose or administered once a week for three weeks via dosed intravenously in mice. SJG-136-induced H2AX phosphorylation shows good correspondence, but less sensitivity, than measurement of foci[2].

Solvent&Solubility

In Vitro:

DMSO : ≥ 100 mg/mL (179.66 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7966 mL	8.9830 mL	17.9659 mL
	5 mM	0.3593 mL	1.7966 mL	3.5932 mL
	10 mM	0.1797 mL	0.8983 mL	1.7966 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 (4.49 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (4.49 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 (4.49 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.49 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 (4.49 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.49 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]. Gregson SJ, et al. Design, synthesis, and evaluation of a novel pyrrolobenzodiazepine DNA-interactive agent with highly efficient cross-linking ability and potent cytotoxicity. J Med Chem. 2001 Mar 1;44(5):737-48. [2]. Mellinas-Gomez M, et al. Activity of the DNA minor groove cross-linking agent SG2000 (SJG-136) against canine tumours. BMC Vet Res. 2015 Aug 19;11:215.

实验参考：

Cell Assay	In vitro cytotoxicity is evaluated using the human ovarian carcinoma cell lines SKOV-3, A2780, and CH1, together with the cisplatin-resistant counterparts of the A2780 and CH1 lines (A2780cisR and CH1cisR, respectively). Viable cells are seeded in growth medium (160 μL) into 96-well microtiter plates and allowed to attach overnight. SJG-136 is dissolved in DMSO (to give a 20 mM concentration in each case) immediately prior to adding to the cells in quadruplicate wells. Final drug concentrations in the wells ranged from 100 μM to 2.5 nM as follows: 100, 25, 10, 2.5, 1 μM, and 250, 100, 25, 10, 2.5 nM. This is achieved by diluting the drugs in growth medium and then adding 40 μL to the existing well volume of 160 μL to give the final concentrations stated above. After 4 days (96 h), the medium is removed and the remaining cells are fixed using 10% trichloroacetic acid on ice for 30 min. Wells are then washed 3−4 times with tap water and air-dried overnight, and 100 μL of 0.4% sulforhodamine B (dissolved in 1% glacial HOAc) is added to each well. Staining is allowed to continue for 10−15 min; the wells are then washed 3−4 times with 1% acetic acid and air-dried, and Tris base (100 μL of 10 mM) is added to each one. The plates are then shaken and absorbance readings taken at 540 nm using a plate reader. From plots of concentration versus percentage absorbance (compared to 8 untreated wells), IC_{50} values are calculated using the Quattro-Pro software package[1].
Animal Administration	A homogenous suspension of 5×10^6 exponentially growing canine melanoma cells in serum free RPMI 1640 tissue culture medium is injected subcutaneously into CD1 Nu/Nu immunocompromised female mice. The mice are divided into five groups of ten mice, with equivalent mean tumour volumes for each group. SJG-136 is given intravenously into the tail vein to four of these groups and vehicle control is administered to the fifth group. SJG-136injections are prepared in 0.9 % NaCl and 1 % DMSO vehicle. Animals are weighed prior to the injection to determine the volume of SJG-136 required (0.1 mL/10 g body weight) which is given IV in the tail vein. Control group mice are given an

	IV injection of the vehicle solution; mice in groups one and two are given a single treatment of SJG-136, 0.15 mg/kg and 0.30 mg/kg respectively; mice in groups four and five are given 0.15 mg/kg and 0.30 mg/kg respectively, every seven days for a total of three treatments[2].
References	[1]. Gregson SJ, et al. Design, synthesis, and evaluation of a novel pyrrolobenzodiazepine DNA-interactive agent with highly efficient cross-linking ability and potent cytotoxicity. J Med Chem. 2001 Mar 1;44(5):737-48. [2]. Mellinas-Gomez M, et al. Activity of the DNA minor groove cross-linking agent SG2000 (SJG-136) against canine tumours. BMC Vet Res. 2015 Aug 19;11:215.