产品名称：GANT61
产品别名：GANT 61

生物活性：

Description	GANT 61 is an inhibitor of Gli1 and Gli2 targeting the Hedgehog/GLI pathway.
IC_{50} & Target	Gli1/2 [1]
In Vitro	GANT61 (20 μM) induces greater cell death than targeting Smo (cyclopamine). GANT61 (0, 5, 10, 20 μM) inhibits clonogenic survival of human colon carcinoma cell lines. GANT61 (20 μM, 0-72 hr) down-regulates Gli1 and Gli2 expression in HT29 cells. GANT61 (0, 10 μM or 20 μM) differentially regulates genes involved in the balance between cell death and cell survival[1]. GANT-61 inhibits cell viability and induces apoptosis in pancreatic CSCs. GANT-61 inhibits expression of downstream targets of Shh pathway, decreases Gli-DNA interaction, Gli transcriptional activity and Gli nuclear translocation in pancreatic CSCs. GANT-61 differentially regulates genes involved in cell survival, cell death and pluripotency. GANT-61 inhibits motility, invasion and migration of CSCs[2]. GANT61 sensitivity positively correlates to GLI1 and negatively to MYCN expression in the neuroblastoma cell lines tested. GANT61 downregulates GLI1, c-MYC, MYCN and Cyclin D1 expression and induces apoptosis of neuroblastoma cells[3].
In Vivo	GANT-61 (40 mg/kg, i.p., three days per week) inhibits CSC tumor growth in NOD/SCID IL2Rγ null mice[2]. GANT61 (50 mg/kg, p.o.) enhances the effects of chemotherapeutic drugs used in the treatment of neuroblastoma in an additive or synergistic manner and reduces the growth of established neuroblastoma xenografts in nude mice[3].

Solvent&Solubility

In Vitro:

DMSO : 25 mg/mL (58.19 mM; Need ultrasonic)

H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3277 mL	11.6387 mL	23.2775 mL
	5 mM	0.4655 mL	2.3277 mL	4.6555 mL
	10 mM	0.2328 mL	1.1639 mL	2.3277 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 (5.82 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (5.82 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 (5.82 mM); Suspended solution; Need ultrasonic 此方案可获得 2.5 mg/mL (5.82 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 (5.82 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.82 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]. Mazumdar T, et al. Hedgehog signaling drives cellular survival in human colon carcinoma cells. Cancer Res. 2011 Feb 1;71(3):1092-102. [2]. Fu J, et al. GANT-61 inhibits pancreatic cancer stem cell growth in vitro and in NOD/SCID/IL2R gamma null mice xenograft. Cancer Lett. 2013 Mar 1;330(1):22-32. [3]. Wickstrom M, et al. Targeting the hedgehog signal transduction pathway at the level of GLI inhibits neuroblastoma cell growth in vitro and in vivo. Int J Cancer. 2013 Apr 1;132(7):1516-24.

实验参考：

Cell Assay	Cells (1.5×10^4) are incubated with 0, 1, 5 and 10 μM of GANT-61 in 250 μL of culture medium in 96-well plate for 48 and 72 h. Cell viability is determined by the XTT assay. In brief, a freshly prepared XTT-PMS labeling mixture (50 μL) is added to the cell culture. The absorbance is measured at 450 nm with λ correction at 650 nm. The cell viability is expressed as ΔOD (OD450 − OD650). The apoptosis is determined by FACS analysis of propidium iodide (PI)-stained cells. In brief, cells are trypsinized, washed with PBS and resuspended in 200 μL PBS with 10 μL RNAase (10 mg/mL) and incubated at 37°C for 30 min. After incubation, 50 μL PI solution is added and cells are analyzed for apoptosis using a flow cytometry. [2]
Animal Administration	Humanized NOD/SCID/IL2Rgammanull mice are used for the assay. Before CSC's injection, mice are humanized with tail vein injection of human normal $CD34^+$ peripheral blood stem/progenitor cells. $CD34^+$peripheral blood stem/progenitor cells (500 cells/mouse, 50-75 μL volume) are injected through tail vein. After 3 days, human pancreatic CSCs (1×10^3 cells mixed with Matrigel, Becton Dickinson, Bedford, MA, in 75 μL total volume, 50:50 ratio) are injected subcutaneously into the flanks of NOD/SCID IL2Rγnull mice (4–6 weeks old). After two weeks of CSC implantation, mice (10 mice per group) are treated with GANT-61(0 and 40 mg/kg body weight) ip three times per week for 6 weeks. At the end of the experiment, mice are euthanized, and tumors are isolated for biochemical analysis. [2]
References	[1]. Mazumdar T, et al. Hedgehog signaling drives cellular survival in human colon carcinoma cells. Cancer Res. 2011 Feb 1;71(3):1092-102. [2]. Fu J, et al. GANT-61 inhibits pancreatic cancer stem cell growth in vitro and in NOD/SCID/IL2R gamma null mice xenograft. Cancer Lett. 2013 Mar 1;330(1):22-32. [3]. Wickstrom M, et al. Targeting the hedgehog signal transduction pathway at the level of GLI inhibits neuroblastoma cell growth in vitro and in vivo. Int J Cancer. 2013 Apr 1;132(7):1516-24.