GANT 61

Cat. No.: HY-13901

CAS No.: 500579-04-4

Molecular Formula: $C_{27}H_{35}N_5$

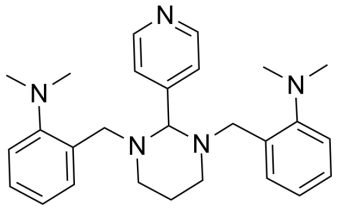
Molecular Weight: 429.6

Target: Gli; Autophagy

Pathway: Stem Cell/Wnt; Autophagy

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

Ethanol : 66.67 mg/mL (155.19 mM; Need ultrasonic)
DMSO : 25 mg/mL (58.19 mM; Need ultrasonic)

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

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: Cremophor EL
   Solubility: 8 mg/mL (18.62 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% EtOH >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 5 mg/mL (11.64 mM); Clear solution
3. Add each solvent one by one: 10% EtOH >> 90% (20% SBE-β-CD in saline)
   Solubility: 5 mg/mL (11.64 mM); Suspended solution; Need ultrasonic
4. Add each solvent one by one: 10% EtOH >> 90% corn oil
   Solubility: ≥ 5 mg/mL (11.64 mM); Clear solution
5. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.82 mM); Clear solution
6. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (5.82 mM); Suspended solution; Need ultrasonic
7. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.82 mM); Clear solution
8. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: ≥ 2.5 mg/mL (5.82 mM); Clear solution

	9. Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline) Solubility: 2.5 mg/mL (5.82 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	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. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	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. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Res. 2022 Mar;32(3):288-301.

- Blood. 2016 Dec 8;128(23):2642-2654.
- Nat Commun. 2023 Jun 24;14(1):3766.
- Nat Commun. 2017 Jun 12;8:15773
- J Clin Invest. 2020 Dec 1;130(12):6354-6365.

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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.

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