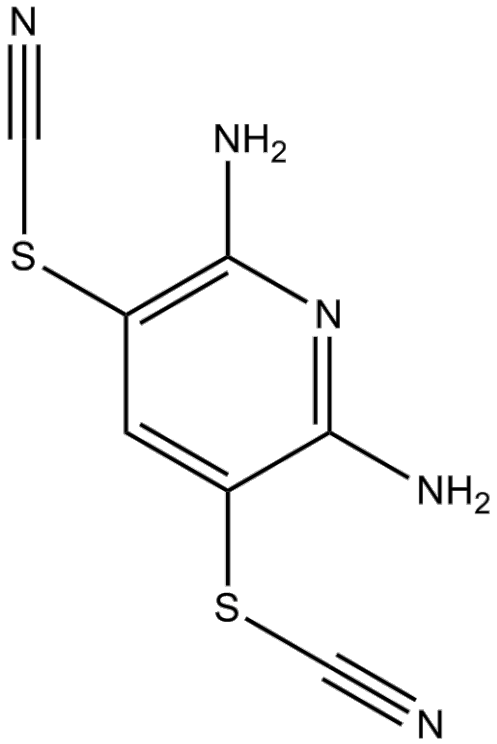
Product Data Sheet

Product Name: PR-619
Cat. No.: GC13208

Chemical Properties

Cas. No.	2645-32-1		
Chemical Name	(2,6-diamino-5-thiocyanatopyridin-3-yl) thiocyanate		
SMILES	C1=C(C(=NC(=C1SC#N)N)N)SC#N		
Formula	$C_7H_5N_5S_2$	M.Wt	223.28
Solubility	≥ 11.15mg/mL in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		

Structure



Protocol

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Cell experiment [1]:

Cell lines	
Preparation Method	T24 and BFTC-905 cells were treated with various concentrations of PR-619 (3-15 μM) for 24 h, 48 h, and 72 h, respectively. Cell viability was assessed using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay.
Reaction Conditions	3-15 μM；24 h, 48 h, and 72 h
Applications	PR-619 effectively induced cytotoxicity and apoptosis in both T24 and BFTC cells in a dose- and time-dependent manner. Additionally, we found that PR-619 induced cytotoxicity in low-grade RT-4 UC cells and cisplatin-resistant UC cells (T24/R) in a dose- and time-dependent manner.

Animal experiment [2]:

Animal models	8-week-old male nude mice
Preparation Method	A total of 5×10^5 JJ012 or SW1353 cells were suspended in 200 μL of serum-free medium and an equal amount of Matrigel. The cell suspension thus derived was then injected subcutaneously into the dorsal side of 8-week-old male nude mice. When the tumor grew to ~150 mm3, mice were randomly assigned to either the PR-619 treatment group or the control group. Mice in the treatment group received PR-619 10 mg/kg intraperitoneal injection twice daily for 48 days. Mice in the untreated control group received an injection of DMSO solution.
Dosage form	10 mg/kg; i.p.

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Applications	PR-619 showed significant anti-tumor effects on xenograft tumors from both cell lines.

References:

[1] Kuo KL, et al. The Deubiquitinating Enzyme Inhibitor PR-619 Enhances the Cytotoxicity of Cisplatin via the Suppression of Anti-Apoptotic Bcl-2 Protein: In Vitro and In Vivo Study. Cells. 2019 Oct 17;8(10):1268.
[2] Lin WC, et al. Anti-tumor effects of deubiquitinating enzyme inhibitor PR-619 in human chondrosarcoma through reduced cell proliferation and endoplasmic reticulum stress-related apoptosis. Am J Cancer Res. 2023 Jul 15;13(7):3055-3066.

Background

PR-619 is a broad-spectrum DUB (deubiquitinating enzyme) inhibitor. PR-619 has demonstrated robust DUB inhibitory activity (5-20 μM) and growth inhibitory activity with IC_{50} of 2 μM in HEK 293T cells[1].

PR-619 at 40 μM induced an above-background TOP2A and TOP2B signal in K562 cells [2]. In vitro efficacy test shown that the anti-tumor effects of PR-619 on the JJ012 and SW1353 human chondrosarcoma cell lines, with PR-619 concentrations ranging from 2.5 to 17.5 μM for 24 and 48 h. PR-619 significantly reduced the viability of chondrosarcoma cells in a dose- and time-dependent manner[3]. In vitro, PR-619 treatment (0 - 80 μM) significantly inhibited cell viability at 24 and 48 h in a dose-dependent manner. Furthermore, PR-619 (20 μM) treatment for 48 h significantly induced apoptosis in cisplatin-resistant T24/R cells[4].

In vivo, mice were intraperitoneally treated with PR-619 (10 mg/kg each day) enhanced the antitumor effect of cisplatin in a xenograft mouse model of T24/R[4].

References:
[1] Altun M, et al. (2011) Activity-based chemical proteomics accelerates inhibitor development for deubiquitylating enzymes. Chem Biol 18:1401-1412

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[2] Cowell IG, et al. The Deubiquitinating Enzyme Inhibitor PR-619 is a Potent DNA Topoisomerase II Poison. Mol Pharmacol. 2019 Nov;96(5):562-572.
[3] Lin WC, et al. Anti-tumor effects of deubiquitinating enzyme inhibitor PR-619 in human chondrosarcoma through reduced cell proliferation and endoplasmic reticulum stress-related apoptosis. Am J Cancer Res. 2023 Jul 15;13(7):3055-3066.
[4] Hsu FS, et al. PR-619, a General Inhibitor of Deubiquitylating Enzymes, Diminishes Cisplatin Resistance in Urothelial Carcinoma Cells through the Suppression of c-Myc: An In Vitro and In Vivo Study. Int J Mol Sci. 2021 Oct 28;22(21):11706.

Caution: Product has not been fully validated for medical applications. For research use only.
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