产品名称：**CX-5461**
产品别名：**CX-5461**

生物活性：	
Description	CX-5461 is a potent and oral rRNA synthesis inhibitor. It inhibits RNA polymerase I-driven transcription of rRNA with IC_{50}s of 142, 113, and 54 nM in HCT-116, A375, and MIA PaCa-2 cells, respectively.
IC_{50} & Target	IC50: 54 nM (rRNA synthesis, MIA PaCa-2 cells), 113 nM (rRNA synthesis, A375 cells), 142 nM (rRNA synthesis, HCT-116 cells)[1]
In Vitro	CX-5461 is a potent and orally bioavailable inhibitor of Pol I-mediated rRNA synthesis, with IC50s of 142 nM in HCT-116, 113 nM in A375, and 54 nM in MIA PaCa-2 cells, and shows little or no effect on Pol II (IC50, ≥25 μM). CX-5461 has modest inhibition on DNA replication and protein translation. CX-5461 also exhibits broad antiproliferative activity against a panel of human cancer cell lines, with a mean EC50 of 147 nM, but has minimal effect on viability of nontransformed human cells, with EC50 values of appr 5000 nM. EC50s of CX-5461 for HCT-116, A375, and MIA PaCa-2 cell lines are 167, 58, and 74 nM, respectively. CX-5461 induces autophagy and senescence in solid tumor cancer cells, rather than apoptosis, through a p53-independent process[1]. Eμ-Myc lymphoma cells from tumor-bearing mice are exquisitely sensitive to CX-5461 with an IC50 of 27.3 nM ± 8.1 nM for Pol I transcription after 1 hr and IC50 of 5.4 nM ± 2.1 nM for cell death after 16 hr. CX-5461 activates p53 via the nucleolar stress response in Eμ-MycLymphoma Cells[2].
In Vivo	CX-5461 displays antitumor activity against human solid tumors in murine xenograft models. CX-5461 (50 mg/kg, p.o.) shows significant MIA PaCa-2 growth inhibition with TGI equal to 69% on day 31 and 79% TGI on A375 on day 32[1]. CX-5461 (50 mg/kg, p.o.) inhibits the Eμ-Myc tumor cells with 84% repression in Pol I transcription at 1 hr posttreatment in C57BL/6 mice. CX-5461 also induces a rapid reduction in tumor burden in the lymph nodes and a concomitant reduction of spleen size to within the normal range[2].
Solvent&Solubility	***In Vitro:*** **DMSO : < 1 mg/mL** (insoluble or slightly soluble)
References	[1]. Drygin D et al. Targeting RNA polymerase I with an oral small molecule CX-5461 inhibits ribosomal RNA synthesis and solid tumor growth. Cancer Res. 2011 Feb 15;71(4):1418-30. [2]. Bywater MJ, et al. Inhibition of RNA Polymerase I as a Therapeutic Strategy to Promote Cancer-Specific Activation of p53. Cancer Cell. 2012 Jul 10;22(1):51-65.

实验参考：	
Cell Assay	Cells are plated on 96-well plates and treated the next day with dose response of CX-5461 for 96 hours. Cell viability is determined using Alamar Blue and CyQUANT assays[1].
Animal Administration	Mice[1] Animal experiments are performed with 5- to 6-week-old female athymic (NCr nu/nu fisol) mice of Balb/c. Mice are inoculated with athymic (NCr nu/nu fisol) mice in 100 μL of cell suspension subcutaneously in the right flank. Tumor measurements are performed by caliper analysis, and tumor volume is calculated using the formula $(l \times w^2)/2$, where w=width and l=length in mm of the tumor. established tumors (appr 110-120 mm^3) are randomized into vehicle (50 mM NaH_2PO_4, pH 4.5), NSC 613327, or CX-5461 treatment groups. Tumor growth inhibition (TGI) is determined on the last day of study according to the formula: TGI (%)=[100 − (Vf^D− Vi^D)/ (Vf^V − Vi^V) × 100], where $Vi^V$is the initial mean tumor volume in vehicle-treated group, Vf^V is the final mean tumor volume in vehicle-treated group, Vi^D is the initial mean tumor volume in drug-treated group, and Vf^D is the final mean tumor volume in drug-treated group.

References	[1]. Drygin D et al. Targeting RNA polymerase I with an oral small molecule CX-5461 inhibits ribosomal RNA synthesis and solid tumor growth. Cancer Res. 2011 Feb 15;71(4):1418-30. [2]. Bywater MJ, et al. Inhibition of RNA Polymerase I as a Therapeutic Strategy to Promote Cancer-Specific Activation of p53. Cancer Cell. 2012 Jul 10;22(1):51-65.

源叶生物