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产品名称：4-(2-氯苯氧基)-N-[3-[(甲胺基)羰基]苯基]-1-哌啶羧胺
产品别名：A939572

生物活性：

Description	A939572 is a potent, and orally bioavailable stearoyl-CoA desaturase1 (SCD1) inhibitor with IC_{50} values of <4 nM and 37 nM for mSCD1 and hSCD1, respectively.
IC_{50} & Target	IC50: <4 nM (mSCD1), 37 nM (hSCD1)[1]
In Vitro	A939572 exhibits robust in vivo activity with dose-dependent desaturation index lowering effects[1]. A939572 is a small molecule that specifically inhibits SCD1 enzymatic activity. A939572 demonstrates a significant dose-dependent decrease in proliferation in Caki1, A498, Caki2, and ACHN at day 5 (IC50s of 65 nM, 50 nM, 65 nM, and 6 nM, respectively). In A939572 (SCDi) treated Caki1 and A498 cells, all five ER stress related genes are expressed at significantly increased levels compared to DMSO+BSA control, and this elevated expression can be blocked with the addition of OA-BSA[2].
In Vivo	Athymic nude (nu/nu) mice bearing A498 ccRCC xenografts are treated with A939572 (30mg/kg, p.o.) and Tem individually or in combination over the course of four weeks, and tumor volume (mm^3) is recorded. A939572 and Tem monotherapy generate similar growth responses with approximately 20-30% reductions in tumor volume (vs. placebo control) being observed upon study completion, with values reaching statistical significance only within the last week of treatment. The combination group yields over a 60% decrease in tumor volume (vs. placebo control) by study completion with significant reductions recorded after approximately 1 week of treatment[2].
Solvent&Solubility	***In Vitro:*** **DMSO : 100 mg/mL** (**257.82 mM;** Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.5782 mL	12.8912 mL	25.7825 mL
	5 mM	0.5156 mL	2.5782 mL	5.1565 mL
	10 mM	0.2578 mL	1.2891 mL	2.5782 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 (6.45 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (6.45 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 (6.45 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.45 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 (6.45 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.45 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]. Xin Z, et al. Discovery of piperidine-aryl urea-based stearoyl-CoA desaturase 1 inhibitors. Bioorg Med Chem Lett. 2008 Aug 1;18(15):4298-302. [2]. von Roemeling CA, et al. Stearoyl-CoA desaturase 1 is a novel molecular therapeutic target for clear cell renal cell carcinoma. Clin Cancer Res. 2013 May 1;19(9):2368-80.

实验参考：

Cell Assay	Cells are plated (0.5 or 1×10^5/well) in 24-well plates in triplicate. Cells are counted using a Coulter Particle Counter. Oleic acid-albumin is added to media at 5μMol. A939572 stocks are prepared in DMSO. Temsirolimus dosing is performed. Soft agar cultures are prepared by diluting 2× growth medium 1:1 in 1.5% Seaplaque®GTG® agarose, with 500 cells/plate in 60mm culture dishes. Colonies are stained with Giemsa and counted after 3wks[2].
Animal Administration	Mice[2] A498 cells are subcutaneously implanted in athymic nu/nu mice at 1×10^6 cells/mouse in 50% Matrigel. Tumors reach ~50 mm^3 prior to 4 wk treatment. A939572 is re-suspended in strawberry flavored Kool-Aid® in sterilized H_2O (0.2 g/mL) vehicle at 30 mg/kg in a 50 μL dose. Mice are orally fed by using a syringe to administer the 50 μL dose twice daily/mouse. This modified method is found to be effective and less stressful on the mice. Temsirolimus is solubilized in 30% ethanol/saline and administered via intraperitoneal injection at 10 mg/kg in a 50 μL dose once every 72 hrs/mouse. Tumor volumes are calculated using the formula 0.5236 (L*W*H) and body weight are measured every 3 days.
References	[1]. Xin Z, et al. Discovery of piperidine-aryl urea-based stearoyl-CoA desaturase 1 inhibitors. Bioorg Med Chem Lett. 2008 Aug 1;18(15):4298-302. [2]. von Roemeling CA, et al. Stearoyl-CoA desaturase 1 is a novel molecular therapeutic target for clear cell renal cell carcinoma. Clin Cancer Res. 2013 May 1;19(9):2368-80.