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产品名称：ZCL278
产品别名：ZCL278

生物活性：

Description	ZCL278 is a selective Cdc42 modulator that directly binds to Cdc42 and inhibits its functions with Kd of 11.4 μM for Cdc42-ZCL278 affinity in surface plasmon resonance (SPR) experiment.
IC_{50} & Target	Kd: 11.4 μM (Cdc42)[1]
In Vitro	ZCL278 as a potent, cell-permeable Cdc42-specific inhibitor that suppresses actin-based cellular functions, including Golgi organization and cell motility.In Swiss 3T3 fibroblast cultures, ZCL278 abolishes microspike formation and disrupted GM130-docked Golgi structures, two of the most prominent Cdc42-mediated subcellular events. ZCL278 reduces the perinuclear accumulation of active Cdc42 in contrast to NSC23766, a selective Rac inhibitor. ZCL278 suppresses Cdc42-mediated neuronal branching and growth cone dynamics as well as actin-based motility and migration in a metastatic prostate cancer cell line (i.e., PC-3) without disrupting cell viability[1]. ZCL278 inhibits Cdc42 function as an entry inhibitor for Junin virus (JUNV) and for vesicular stomatitis virus, lymphocytic choriomeningitis virus, and dengue virus but not for the nonenveloped poliovirus. In cells, ZCL278 is shown to efficiently inhibit chemically induced filopodium formation, a process dependent on Cdc42 activity. Dose-response experiments are first carried out in Vero cells, and while ZCL278 is not toxic at concentrations up to 200 μM, ZCL278 inhibits JUNV with IC50 of ~14 μM, as measured by flow cytometry[2].
In Vivo	ZCL278 reduces the JUNV RNA load in the spleen more than 33-fold, with JUNV RNA being undetectable in 5 out of 8 mice. These results are similar to those seen in Gabapentin-treated mice, demonstrating that ZCL278 can abrogate JUNV replication[2].
Solvent&Solubility	***In Vitro:*** **DMSO : 50 mg/mL (85.49 mM;** Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7097 mL	8.5486 mL	17.0972 mL
	5 mM	0.3419 mL	1.7097 mL	3.4194 mL
	10 mM	0.1710 mL	0.8549 mL	1.7097 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 (4.27 mM); Clear solution

	此方案可获得 ≥ 2.5 mg/mL (4.27 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% corn oil Solubility: ≥ 2.5 mg/mL (4.27 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.27 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]. Friesland A, et al. Small molecule targeting Cdc42-intersectin interaction disrupts Golgi organization and suppresses cell motility. Proc Natl Acad Sci U S A. 2013 Jan 22;110(4):1261-6. [2]. Chou YY, et al. Identification and Characterization of a Novel Broad-Spectrum Virus Entry Inhibitor. J Virol. 2016 Apr 14;90(9):4494-510.

实验参考：

Cell Assay	To determine cell viability, PC-3 cells are incubated for 24 h with or without the Cdc42 activator, ZCL278, or NSC23766. By using the trypan blue dye exclusion method, the numbers of live and dead cells are obtained with a Countess Automated Cell Counter. P values are assigned in each experiment, and any null hypothesis with probability level <95% is rejected[1].
Animal Administration	Mice[2] Four-week-old C57BL/6 mice receive intravenous injections of Gabapentin or ZCL278 (100 μg/g, i.p.). At 1 h after treatment, the mice are inoculated intraperitoneally with JUNV Candid #1 (1×10^6 PFU) in no more than 1 mL with a 27 1/2-gauge needle. At the end of the experiment, the mice are sacrificed, their spleens are homogenized with a Dounce homogenizer and centrifuged to generate a cell pellet and supernatant, and RNA expression levels are determined.
Kinase Assay	Lyophilized Cdc42 protein is reconstituted to 5 mg/mL in a buffer consisting of 50 mM Tris, 0.5 mM MgCl2, 50 mM NaCl, 3% (wt/vol) sucrose, and 0.6% dextran. The stock solution is then diluted to 1 μM in 5 mM phosphate buffer, pH 7.4. Into a quartz cuvettete containing Cdc42 solution, aliquots of ZCL278 are added and incubated for 5 min before each fluorescent measurement. The excitation wavelength is 275 nm, and the fluorescence of tryptophan at 350 nm is measured after each addition. The titration curve is fitted using the equimolar specific binding model in GraphPad, and the Kd is calculated[1].
References	[1]. Friesland A, et al. Small molecule targeting Cdc42-intersectin interaction disrupts Golgi organization and suppresses cell motility. Proc Natl Acad Sci U S A. 2013 Jan 22;110(4):1261-6. [2]. Chou YY, et al. Identification and Characterization of a Novel Broad-Spectrum Virus Entry Inhibitor. J Virol. 2016 Apr 14;90(9):4494-510.