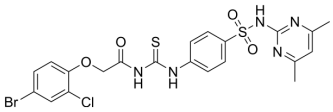
ZCL278

Cat. No.:	HY-13963
CAS No.:	587841-73-4
Molecular Formula:	$C_{21}H_{19}BrClN_5O_4S_2$
Molecular Weight:	584.89
Target:	Ras; Flavivirus; Dengue virus; VSV
Pathway:	GPCR/G Protein; Anti-infection
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



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

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (4.27 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.27 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

ZCL278 is a selective Cdc42 modulator that directly binds to Cdc42 and inhibits its functions with K_d 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 IC_{50} of ~14 μM, as measured by flow cytometry[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	Lyophilized Cdc42 protein is reconstituted to 5 mg/mL in a buffer consisting of 50 mM Tris, 0.5 mM $MgCl_2$, 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 K_d is calculated[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [1]	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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	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. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Mol Immunol. 2020 May;17(5):496-506.
- FASEB J. 2021 Apr;35(4):e21554.

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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.

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

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