

产品名称: DEL-22379

产品别名: DEL-22379

生物活性:

Description	DEL-22379 is an ERK dimerization Inhibitor. DEL-22379 readily binds to ERK2 with a Kd estimated in the low micromolar range, though binding is detectable even at low nanomolar concentrations. ERK2 dimerization is progressively inhibited with an IC50 of ~0.5 μM.				
IC50 & Target	ERK2				
	0.5 μM (IC50)				
In Vitro	DEL-22379 is an ERK dimerization inhibitor. DEL-22379 abolishes EGF-induced co-immunoprecipitation of ectopic ERK2 molecules tagged with hemagglutinin (HA) or FLAG epitopes, with an estimated half-maximal inhibitory concentration (IC50) of ~0.5 μM. DEL-22379 inhibits growth of tumor cells harboring RAS-ERK pathway oncogenes. The biological effects of DEL-22379 are investigated on tumor cells in culture. The cytostatic effects of DEL-22379 are compared to those of the MEK inhibitor PD-0325901 and the ERK kinase inhibitor SCH-772984, as reflected by their half-maximal growth inhibitory concentrations (GI50). Cell lines harboring mutant BRAF are the most sensitive to the three compounds. In comparison, wild-type (WT) cell lines for BRAF and RAS are the most resistant, and RAS mutant cells exhibit a range of sensitivities. In cells showing different oncogenic genotypes, distinct sensitivity to DEL-22379 can not be attributed to variations on its effects on dimerization, because DEL-22379 displays similar dimerization- and cytoplasmic signaling-inhibitory dose responses (IC50 of 150-400 nM) regardless of the genotype[1].				
In Vivo	To test DEL-22379 antitumor effects, some of the aforementioned cell lines are xenografted into nude mice, and tumor growth is monitored after intra-peritoneal administration of DEL-22379 at 15 mg/kg. At such a dose, inhibition of ERK dimerization is evident in liver extracts and in xenografted tumors. DEL-22379 markedly inhibits tumor progression for A375 cells (BRAF mutant)[1].				
Solvent&Solubility	<b>In Vitro:</b> <b>DMSO : ≥ 30 mg/mL (67.49 mM)</b>  * "≥" means soluble, but saturation unknown.				
	Preparing Stock Solutions	<div>Solvent / Mass / Concentration</div>	1 mg	5 mg	10 mg
		1 mM	2.2496 mL	11.2478 mL	22.4957 mL
		5 mM	0.4499 mL	2.2496 mL	4.4991 mL
		10 mM	0.2250 mL	1.1248 mL	2.2496 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℃, 6 months; -20℃, 1 month。 -80℃ 储存时, 请在 6 个月内使用, -20℃ 储存时, 请在 1 个月内使用。				
References	[1]. Herrero A, et al. Small Molecule Inhibition of ERK Dimerization Prevents Tumorigenesis by RAS-ERK Pathway Oncogenes. Cancer Cell. 2015 Aug 10;28(2):170-82.				

实验参考:

Cell Assay	HEK293T cells are plated at a density of 1,000-2,000 cells/well and treated with DEL-22379 (0.2-1 μM) for 48 hr, Alamar Blue is added, and the colorimetric change is measured at 570 and 600 nm. GI50 is estimated by nonlinear regression using GraphPad5 Prism Software. Apoptosis is analyzed
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	by evaluating caspase 3 activity, either by western blotting or using the Caspase-Glo 3/7 luminogenic assay[1].
<b>Animal Administration</b>	<p>Mice[1]</p> <p>Cancer cells are xenografted in female, athymic nu/nu mice of 8 weeks of age. <math>3 \times 10^6</math> cells are injected subcutaneously in the lateral flank and allowed to develop for 10-15 days before treatment with DEL-22379 at 15 mg/kg every 12 hr for 2 weeks. patient-derived xenografts (PDXs) are performed using patient-derived colorectal cancer cells harboring BRAFV600E from non-necrotic areas of primary adenocarcinomas from patients that undergo surgical resection. Cells are grafted in both flanks or in the cecum of NOD-SCID mice. DEL-22379 is administered by intra-peritoneal injection at a concentration of 15 mg/kg every 12 hr for 30 days[1].</p>
<b>References</b>	[1]. <u>Herrero A, et al. Small Molecule Inhibition of ERK Dimerization Prevents Tumorigenesis by RAS-ERK Pathway Oncogenes. Cancer Cell. 2015 Aug 10;28(2):170-82.</u>



源叶生物