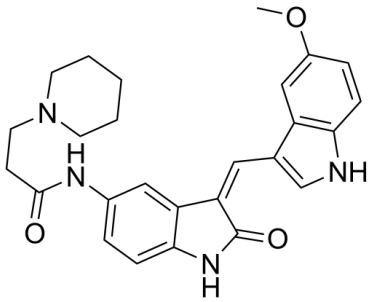
Data Sheet

Product Name:	DEL-22379
Cat. No.:	CS-5355
CAS No.:	181223-80-3
Molecular Formula:	$C_{26}H_{28}N_4O_3$
Molecular Weight:	444.53
Target:	Apoptosis; ERK
Pathway:	Apoptosis; MAPK/ERK Pathway; Stem Cell/Wnt
Solubility:	DMSO : 100 mg/mL (ultrasonic)



BIOLOGICAL ACTIVITY:

DEL-22379 is an **ERK dimerization** Inhibitor. DEL-22379 readily binds to ERK2 with a K_d estimated in the low micromolar range, though binding is detectable even at low nanomolar concentrations. **ERK2 dimerization** is progressively inhibited with an **IC_{50}** of ~0.5 μM. IC50 & Target: IC50: ~0.5 μM (ERK2 dimerization)[1] ***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 (IC_{50}) 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 (GI_{50}). 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 (IC_{50} 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].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: [1]**HEK293T cells** are plated at a density of 1,000-2,000 cells/well and treated with **DEL-22379 (0.2-1 μ M)** for 48 hr, Alamar Blue is added, and the colorimetric change is measured at 570 and 600 nm. GI_{50} is estimated by nonlinear regression using GraphPad5 Prism Software. Apoptosis is analyzed by evaluating caspase 3 activity, either by western blotting or using the Caspase-Glo 3/7 luminogenic assay[1].

Animal Administration: [1]Mice[1]

Cancer cells are xenografted in **female, athymic nu/nu mice** of 8 weeks of age. 3×10^6 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].

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.

CAIndexNames:

1-Piperidinepropanamide, N-[2,3-dihydro-3-[(5-methoxy-1H-indol-3-yl)methylene]-2-oxo-1H-indol-5-yl]-

SMILES:

O=C(CCN1CCCCC1)NC2=CC=C(NC(/C3=C\C4=CNC5=C4C=C(OC)C=C5)=O)C3=C2

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