

Product Data Sheet

Product Name: DEL-22379

Cat. No.: GC16214

Chemical Properties

Cas. No. 181223-80-3

Chemical Name N-(3-((5-methoxy-1H-indol-3-yl)methylene)-2-oxoindolin-5-yl)-3-(piperidin-1-yl)propanamide

SMILES O=C1NC2=CC=C(NC(CCN3CCCCC3)=O)C=C2C1=CC4=CNC5=CC=C(OC)C=C54

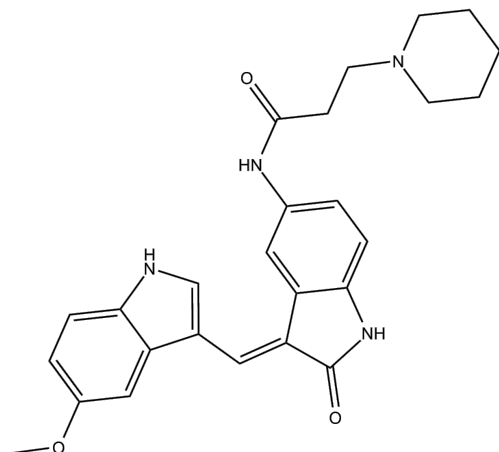
Formula $C_{26}H_{28}N_4O_3$ M.Wt 444.53

Solubility DMF: 30 mg/ml, DMSO: 30 mg/ml, DMSO:PBS(pH 7.2) (1:3): 0.25 mg/ml, Ethanol: slightly soluble
Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution: ship with blue ice. All other available size: ship with RT, or blue ice upon request.

Structure



Protocol

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

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Cell experiment: 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. GI50 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 experiment: 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.

Background

DEL-22379 is an inhibitor of the dimerization of ERK with IC50 values ranging from 150-400 nM regardless of genotypes in oncogenic cells [1].

As an spatial regulator of ERK signals, ERK dimerization is essential. Impeding ERK dimerization can result in the impeding of ERK signals' extranuclear component and hence result in curtailing tumor development and cellular transformation [1].

In HEK293 cells, DEL-22379 abolished EGF-stimulated ERK dimerization. In these cells, the EGF-

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induced co-immunoprecipitation of hemagglutinin- or FLAG epitopes- tagged ectopic ERK2 molecules, was abolished by DEL-22379 with an IC₅₀ value of ~0.5 μ M. In both assays, the inhibition of DEL-22379 to ERK dimerization was not associated with ERK phosphorylation. In the cytoplasm of EGF-stimulated HeLa cells, ERK dimerization was prominent, but previous treatment with DEL-22379 also resulted in no detected ERK dimers [1].

In nude mice with some of the aforementioned tumor cell lines, DEL-22379 at a dose of 15 mg/kg inhibited ERK dimerization evidently in xenografted tumors and in liver extracts. DEL-22379 inhibited the tumor progression of A375 cells (BRAF mutant) markedly. Activated-RAS-driven tumors were very sensitive to DEL-22379. Data indicated that tumorigenesis had greater requirements for ERK dimerization than for proliferation. In tumors, treatment with DEL-22379 resulted in extensive mucinous differentiation and cell death [1].

Reference:

[1]. Herrero A, Pinto A, Colón-Bolea P, et al. Small molecule inhibition of ERK dimerization prevents tumorigenesis by RAS-ERK pathway oncogenes. *Cancer cell*, 2015, 28(2): 170-182.

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