
Product Data Sheet

Product Name: Deltarasin
 Cat. No.: GC13076

Chemical Properties

Cas. No. 1440898-61-2

Chemical Name (S)-1-benzyl-2-(4-(2-(2-phenyl-1H-benzo[d]imidazol-1-yl)-2-(piperidin-4-yl)ethoxy)phenyl)-1H-benzo[d]imidazole

SMILES [H][C@@](C1CCNCC1)(N2C3=CC=CC=C3N=C2C4=CC=CC=C4)COC5=CC=C(C6=NC7=CC=CC=C7N6CC8=CC=CC=C8)C=C5

Formula C₄₀H₃₇N₅O M.Wt 603.75

Solubility Soluble in DMSO Storage Store at -20°C

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

Structure

Protocol

Kinase experiment:

K_d values are measured by fluorescence polarization measurements. For direct titrations, increasing amounts of PDEδ are added to a solution containing 50-100 nM labelled small molecule in 200 μL PBS buffer. For displacement titrations, increasing amounts of the small molecules in DMSO are directly added to fluorescein-labelled atorvastatin (24 nM) and His6-tagged PDEδ (40 nM) in 200 μL PBS-buffer (containing 0.05% CHAPS, 1% DMSO), keeping the concentration of fluorescein-labelled atorvastatin, PDEδ and DMSO constant. For K_d measurements using isothermal titration calorimetry, PDEδ protein (280 μM) is titrated to small molecule (30 μM) in Tris/HCl buffer (temperature 25°C). In the T_m shift assays, protein melting points are detected by circular dichroism spectroscopy in the presence of small molecules.

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

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References:

- [1]. Zimmermann G, et al. Small molecule inhibition of the KRAS-PDE δ interaction impairs oncogenic KRAS signalling. Nature. 2013 May 30;497(7451):638-42.
- [2]. Agaloti T, et al. Mutant KRAS promotes malignant pleural effusion formation. Nat Commun. 2017 May 16;8:15205. doi: 10.1038/ncomms15205.

Background

The KRAS oncogene product is considered a major target in anticancer drug discovery. Interfering with binding of mammalian PDE δ to KRAS by means of small molecules provides a novel opportunity to suppress oncogenic RAS signalling by altering its localization to endomembranes. Deltarasin is an inhibitor of the KRAS-PDE δ interaction to impair oncogenic KRAS signalling.

In vitro: Within a minute, 5 mM of deltarasin completely inhibited PDE δ -KRAS interaction and released the insolubilized mCitrine-RHEB/KRAS6Q to the endomembrane system. This showed that deltarasin interfered with the binding of KRAS to PDE δ in cells and thereby inhibited its solubilization [1].

In vivo: A clear dose-dependent reduction in Panc-Tu-1 tumour growth rate could be observed in deltarasin treated mice with respect to the vehicle-injected controls, where the growth of tumours in mice that were treated with 10mg kg/1 BID deltarasin was almost completely blocked [1].

Clinical trial: No clinical data are available.

Reference:

- [1] Zimmermann G, Papke B, Ismail S, Vartak N, Chandra A, Hoffmann M, Hahn SA, Triola G, Wittinghofer A, Bastiaens PI, Waldmann H. Small molecule inhibition of the KRAS-PDE δ interaction impairs oncogenic KRAS signalling. Nature. 2013;497(7451):638-42.

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