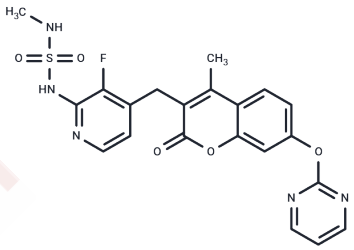
Data Sheet (Cat.No.T6971)

TargetMol

Ro 5126766

Chemical Properties



CAS No. : 946128-88-7

Formula: C21H18FN5O5S

Molecular Weight: 471.46

Appearance: no data available

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	RO5126766 (CH5126766) is a dual RAF/MEK inhibitor with IC50 of 8.2 nM, 19 nM, 56 nM, and 160 nM for BRAF V600E, BRAF, CRAF, and MEK1, respectively. Phase 1.
Targets(IC50)	Raf,MEK
In vitro	In HCT116 KRAS-mutant colorectal cancer cells, CH5126766 significantly reduces the levels of phospho-MEK and phospho-ERK. CH5126766 inhibits RAF kinase by binding to MEK1, and causes MEK to become a dominant negative inhibitor of RAF. [1] In Raf or RAS-mutant cell lines SK-MEL-28, SK-MEL-2, MIAPaCa-2, SW480, HCT116, and PC3 cells, CH5126766 inhibits cell growth with IC50 of 65, 28, 40, 46, and 277 nM, respectively. In two melanoma cell lines with the BRAF V600E or NRAS mutation, RO5126766 induces G1 cell cycle arrest accompanied by up-regulation of the CDK inhibitor p27 and down-regulation of cyclinD1. [3]
In vivo	In an HCT116 (G13D KRAS) mouse xenograft model, CH5126766 (25 mg/kg, p.o.) inhibits ERK signaling output more effectively than a standard MEK inhibitor that induces MEK phosphorylation and has potent antitumor activity. [1] In the HCT116 (K-ras) and COLO205 (B-raf) mutant xenografts, CH5126766 (0.3 mg/kg) causes significant decreases in [18?F]FDG uptake. [2] In the SK-MEL-2 xenograft model, RO5126766 also suppresses the tumor growth. [3]
Kinase Assay	MEK and RAF kinase enzyme assays: The inhibitory activities against CRAF, BRAF, or BRAF V600E enzymes are measured by quantification of phosphorylation of inactive K97R MEK1 [MEK1] by recombinant RAF proteins [BRAF: B-RAF wt, BRAF V600E: B-RAF V600E or CRAF: Raf-1] with Europium-anti-MEK1/2 (pSer218/222) antibody and SureLight allophycocyanine-anti-6his antibody by measuring time-resolved fluorescence (TRF). Alternatively, the inhibitory activities against the RAF enzymes are measured by quantification of phosphorylation of a fluorescein-labeled peptide corresponding to human MEK1 212-224 and human MEK2 217-229 (5-Fl-SGQLIDSMANSFV-NH2, MEKtide) by using the IMAP fluorescence polarization (FP) Screening Express Kit. Inhibition of MEK1 is evaluated by a coupled assay with active MEK1 (MEK1 S218E/S222E) and unactive dephosphorylated ERK2 (MAP kinase 2/Erk 2). The phosphorylation of a fluorescent-labeled peptide substrate (FAM-Erktide, IPTTPITTTYFFFK-5FAM-COOH) by ERK2 is quantified by using the IMAP FP Screening Express Kit.

Cell Research	The number of viable cells is determined using the Cell Counting Kit-8 assay according to the manufacturer's instructions. After the incubation of cells for 72 h with the indicated concentrations of various agents, kit reagent WST-8 is added to the medium and incubated for a further 4 h. The absorbance of samples (450 nm) is determined using a scanning multiwell spectrophotometer that serves as an ELISA reader. Cell numbers and viability are also measured using the ViaCount Assay according to the manufacturer's instructions.(Only for Reference)

Solubility Information

Solubility	DMSO: 87 mg/mL (184.53 mM),Sonication is recommended. Ethanol: < 1 mg/mL (insoluble or slightly soluble), H2O: < 1 mg/mL (insoluble or slightly soluble), (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.1211 mL	10.6054 mL	21.2107 mL
5 mM	0.4242 mL	2.1211 mL	4.2421 mL
10 mM	0.2121 mL	1.0605 mL	2.1211 mL
50 mM	0.0424 mL	0.2121 mL	0.4242 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Reference

Ishii N, et al. Cancer Res. 2013, 73(13), 4050-4060.
Miller CR, et al. Gynecol Oncol. 2014, 133(1), 128-137.
Wada M, et al. PLoS One. 2014, 9(11), e113217.