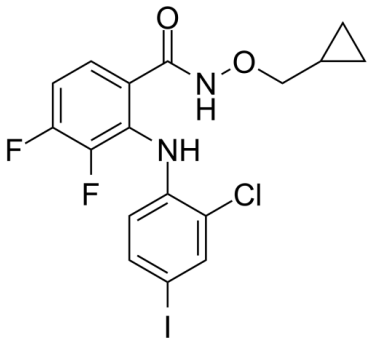
Data Sheet

Product Name:	CI-1040
Cat. No.:	CS-0058
CAS No.:	212631-79-3
Molecular Formula:	$C_{17}H_{14}ClF_2IN_2O_2$
Molecular Weight:	478.66
Target:	Apoptosis; MEK
Pathway:	Apoptosis; MAPK/ERK Pathway
Solubility:	DMSO : ≥ 100 mg/mL (208.92 mM)



BIOLOGICAL ACTIVITY:

CI-1040 (PD 184352) is an orally active, highly specific, small-molecule inhibitor of **MEK** with an **IC_{50}** of 17 nM for MEK1. IC50 & Target: IC50: 17 nM (MEK)[1] **In Vitro:** CI-1040 directly inhibits MEK1 with an IC_{50} of 17 nM. It has also been shown to have little activity against a panel of related kinases with IC_{50} values more than 2.5 orders of magnitude higher. Treatment of whole cells with CI-1040 completely inhibits the mitogen-stimulated phosphorylation of ERK. CI-1040 at a concentration of 1 μM is found to inhibit phosphorylation of ERK1 and ERK2 by 99% and 92%, respectively in MDA-MB-231 breast cancer cells[1]. CI-1040 induces apoptosis and inhibits proliferation in U-937 cells in a dose and time-dependent manner. CI-1040 induces a significant increase in PUMA mRNA and protein levels[2]. **In Vivo:** The systemic administration of the MEK inhibitor CI-1040 reduces adenoma formation to a third and significantly restores lung structure. The proliferation rate of lung cells of mice treated with CL-1040 is decreased without any obvious effects on differentiation of pneumocytes[3].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: [2]The MEK inhibitor CI-1040 is dissolved in DMSO as 10 mM stock solutions and used in cell culture at final concentration 50 mg/mL. U-937 cells are pretreated for 24 hrs with 5 and 20 uM CI- 1040, then transfected with wt-p53 siRNA or PUMA siRNA for 48 hrs. Then 20 mL of MTT solution are added to each well and incubated further for 2 hours. Upon termination, the supernatant is aspirated and the MTT formazan formed by metabolically viable cells is dissolved in 100 mL of isopropanol. The plates are mixed for 30 minutes on a gyratory shaker, and absorbance is measured at 595 nm using a plate reader[2]. **Animal Administration:** [3]Mice: The lung cancer mouse model is generated by targeting constitutively active C-Raf kinase to the lung. BAY 43-9006 or CI-1040 is daily intraperitoneal injected at a dose of 100 mg/kg from 4 months of age over a period of 21 days. Lungs were isolated and analyzed at the end of the treatment period[3].

References:

[1]. Allen LF, et al. CI-1040 (PD184352), a targeted signal transduction inhibitor of MEK (MAPKK). Semin Oncol. 2003 Oct;30(5 Suppl 16):105-16.

[2]. Wei CR, et al. MEK inhibitor CI-1040 induces apoptosis in acute myeloid leukemia cells in vitro. Eur Rev Med Pharmacol Sci. 2016 May;20(10):1961-8.

[3]. Kramer BW, et al. Use of mitogenic cascade blockers for treatment of C-Raf induced lung adenoma in vivo: CI-1040strongly reduces growth and improves lung structure. BMC Cancer. 2004 Jun 1;4:24.

CAIndexNames:

Benzamide, 2-[(2-chloro-4-iodophenyl)amino]-N-(cyclopropylmethoxy)-3,4-difluoro-

SMILES:

O=C(C1=CC=C(C(F)=C1NC2=CC=C(I)C=C2Cl)F)NOCC3CC3

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