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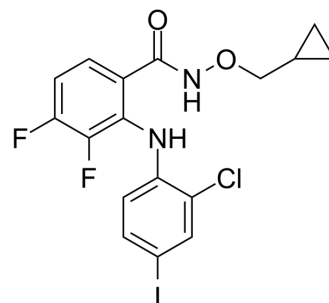
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CI-1040

Cat. No.:	HY-50295
CAS No.:	212631-79-3
Molecular Formula:	C ₁₇ H ₁₄ ClF ₂ IN ₂ O ₂
Molecular Weight:	478.66
Target:	MEK; Apoptosis
Pathway:	MAPK/ERK Pathway; Apoptosis
Storage:	<div>Powder</div> <div>-20°C 3 years</div> <div>4°C 2 years</div> <div>In solvent</div> <div>-80°C 1 year</div> <div>-20°C 6 months</div>



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (208.92 mM)
 * "≥" means soluble, but saturation unknown.

	Solvent Concentration	Mass	1 mg	5 mg	10 mg
Preparing Stock Solutions	1 mM		2.0892 mL	10.4458 mL	20.8917 mL
	5 mM		0.4178 mL	2.0892 mL	4.1783 mL
	10 mM		0.2089 mL	1.0446 mL	2.0892 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
 Solubility: ≥ 2.5 mg/mL (5.22 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil
 Solubility: ≥ 2.08 mg/mL (4.35 mM); Clear solution

BIOLOGICAL ACTIVITY

Description	CI-1040 (PD 184352) is an orally active, highly specific, small-molecule inhibitor of MEK with an IC ₅₀ of 17 nM for MEK1.
IC ₅₀ & Target	MEK1 17 nM (IC ₅₀)
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].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

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].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

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].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nat Methods. 2023 Nov 2.
- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Clin Cancer Res. 2020 Apr 15;26(8):2011-2021.
- Int J Biol Macromol. 2020 May 1;150:261-280.
- Int J Biol Macromol. 2018 Dec;120(Pt A):1039-1047.

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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-1040 strongly reduces growth and improves lung structure. BMC Cancer. 2004 Jun 1;4:24.

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

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