For Research Use Only

CI-1040

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Catalog Number: CM05059

产品信息

Catalog Number:
CM05059

CAS号:
212631-79-3

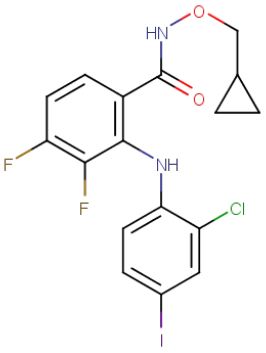
分子式:
$C_{17}H_{14}ClF_2IN_2O_2$

主要靶点:
MEK|Apoptosis

主要通路:
MAPK信号通路|凋亡

分子量:
478.67

溶解度:
Ethanol:12 mg/mL (25 mM),DMSO:47.9 mg/mL (100 mM)



靶点活性

MEK1:17 nM (cell free)|MEK2:17 nM (cell free)

体外活性

PD 184352 (CI-1040) also substantially reduced steady-state levels of phosphorylated MAPK (pMAPK) in a diverse panel of tumor lines grown in the presence of serum. Treatment of colon 26 cells for 1 hour with 1 μM PD 184352 produced a reduction of pMAPK levels of more than 75%. Treatment of colon 26 cells with 10 μM PD 184352 did not inhibit the phosphorylation of Jun kinase, p38 kinase or AKT [1]. The IC50 for inhibition of MKK1 by PD 184352 was 0.3 μM, 15-fold higher than the concentration required to inhibit the EGF-induced activation of ERK2 in Swiss 3T3 cells. The activation of MKK1 in cells was inhibited by 50% at 2 nM PD 184352 [2]. CI-1040 induced apoptosis and inhibited proliferation in U-937 cells in a dose and time-dependent manner. CI-1040 induced a significant increase in PUMA mRNA and protein levels. Knockdown of PUMA by PUMA siRNA transfection inhibited CI-1040-induced apoptosis and proliferation inhibition in U-937 cells [3].

体内活性

The tumors were excised at 1 hour and 6 hours after treatment with PD 184352 (150 mg/kg, i.p. or p.o.). Treatment with PD 184352 completely suppressed MAPK phosphorylation by either route of administration for at least 6 hours. MAPK phosphorylation returned at 12 hours after dosing and attained control levels by 24 hours [1]. In vivo, the systemic administration of the MEK inhibitor CI-1040 reduced adenoma formation to a third and significantly restored lung structure. The proliferation rate of lung cells of mice treated with CL-1040 was decreased without any obvious effects on the differentiation of pneumocytes [4].

动物实验

Tumor fragments (approximately 3 mm^3 in size) were implanted subcutaneously into the right axillae of CD2F1 male mice (colon 26 studies) or female nude mice (HT-29 studies) 4–6 weeks old. Treatment was administered by gavage or intraperitoneally and was initiated either the day after tumor implantation (colon 26) or when tumors reached approximately 200 mg in size (HT-29). PD 184352 was prepared in a vehicle of 10% Cremophore EL, 10% ethanol and 80% water. Tumor size was evaluated periodically by caliper measurements, generally three times per week. Percent tumor growth inhibition was calculated as [(T–C)/number of days of treatment] × 100, with T and C being defined as the time required for treated and control tumors, respectively, to reach 750 mg (colon 26) or to reach twofold growth (HT-29) [1].

细胞实验

Cells were planted seeded in T-75 cm2 flasks and treated the next day for 24 h with either DMSO or PD 184352. Single-cell suspensions were collected, and pellets were fixed in ice-cold ethanol (70%) for 30 min. After centrifugation of the samples, propidium iodide (50 μg/ml) and RNase (30 units/ml) were added to the pellets for 20 min at 37 °C. After filtration, samples were analyzed by flow cytometry [1].

描述

CI-1040 (PD184352) is an ATP non-competitive MEK1/2 inhibitor (IC50: 17 nM).

储存

Powder: -20°C for 3 years | In solvent: -80°C for 2 years