For Research Use Only

Selisistat

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Catalog Number: CM00041

产品信息

Catalog Number:
CM00041

CAS号:
49843-98-3

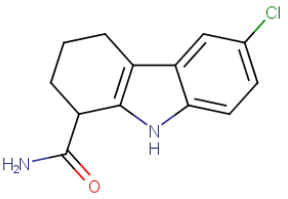
分子式:
$C_{13}H_{13}ClN_2O$

主要靶点:
Sirtuin

主要通路:
DNA损伤和修复|表观遗传

分子量:
248.71

溶解度:
DMSO:18.7 mg/mL (75 mM),Ethanol:12.4 mg/mL (50 mM)



靶点活性

SIRT1:38 nM(cell free)

体外活性

Treatment with Selisistat (EX-527) dramatically increased acetylation at lysine 382 of p53 after different types of DNA damage in primary human mammary epithelial cells and several cell lines. Inhibition of SIRT1 catalytic activity by EX-527 had no effect on cell growth, viability, or p53-controlled gene expression in cells treated with etoposide [1]. When the function of SIRT1 is inhibited by EX527 or its expression is suppressed by RNAi, the upregulated level and release of IL-1β and TNF-α by high glucose are further increased [2]. When HCT116 cells were cultured in 0.1% serum, addition of EX-527 caused a 90% increase in cell number after 7 days. In the presence of 10% serum, EX-527 did not change cell number in long term culture [3].

体内活性

The central pretreatment with Ex527 blunted the ghrelin-induced food intake in rats. Mice lacking p53, a target of SIRT1 action, failed to respond to ghrelin in feeding behavior. Ghrelin failed to phosphorylate hypothalamic AMPK when rats were pretreated with Ex527, as it did in p53 KO mice [4]. EX-527 abolished RSV-induced attenuation of microvascular inflammation in ob/ob septic mice [5].

动物实验

Mice were injected with RSV (RSV) 30mg/kg (4ml/kg) or equivalent volume of DMSO (Vehicle) (4ml/kg) intraperitoneally 18 hours pre-sepsis. This dose of RSV in mice was as per documented literature. In one group of mice, RSV pre-treated mice received EX-527 (10 mg/kg intraperitoneally; 4ml/kg, Vehicle: DMSO) within 10 minutes of cecal ligation and puncture [5].

细胞实验

NCI-H460 cells, MCF-7 cells, U-2 OS cells, or HMEC were plated at 2,000 cells per well in opaque-walled 96-well plates for the viability assay and 800 cells per well in 96-well Cytostar-T scintillating microplates for the proliferation assay. Cells were incubated for 1 day (NCI-H460) or 2 days (MCF-7, U-2 OS, and HMEC) prior to exposure to DNA-damaging agents and deacetylase inhibitors. All experiments were performed in triplicate. For viability assays, cells were treated with the indicated compounds for 48 h. Cell viability was then determined using the Cell Titer-Glo luminescent assay, which measures total ATP levels as an index of cell number. Luminescence was measured on a Luminoskan Ascent. For the proliferation assay, 0.5 μCi/ml of [14C]thymidine was added to the medium immediately after the genotoxins and deacetylase inhibitors. Plates were counted at 48 h (HMEC) or 72 h (NCI-H460, MCF-7, and U-2 OS cells) in a Microbeta liquid scintillation counter. Thymidine incorporated by the cells was detected by proximity to the scintillant in the base of the Cytostar-T tissue culture plate [1].

描述

EX 527 is an effective and specific SIRT1 inhibitor (IC50: 38 nM) and shows >200-fold selectivity against SIRT2/3.

储存

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