For Research Use Only

Adezmapimod

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Catalog Number: CM05675

产品信息

Catalog Number:
CM05675

CAS号:
152121-47-6

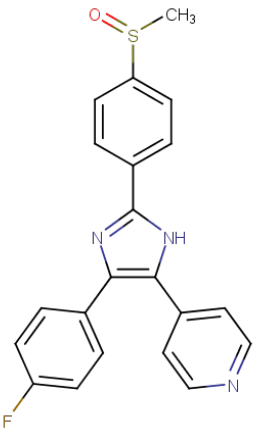
分子式:
$C_{21}H_{16}FN_3OS$

主要靶点:
p38 MAPK|Mitophagy|Autophagy

主要通路:
MAPK信号通路|自噬

分子量:
377.43

溶解度:
1eq. HCl:37.7 mg/mL (100 mM),DMSO:9.4 mg/mL (25 mM)



靶点活性

p38 MAPK:0.3-0.5 μM (THP-1 cells)|PKB:3-5 μM (THP-1 cells)

体外活性

The concentrations of SB203580 required to block PKB phosphorylation (IC50: 3-5 μM) are only approximately 10-fold higher than those required to inhibit p38 MAP kinase (IC50: 0.3-0.5 μM) [1]. SB 203580 inhibits RK in vitro (IC50: 0.6 μM), suppresses the activation of MAPKAP kinase-2 and prevents the phosphorylation of heat shock protein (HSP) 27 in response to interleukin-1 [2]. Pretreatment with the p38 MAPK specific inhibitor SB203580 (1 μM) or overexpression of kinase-deficient mutants of MKK3 or MKK6 did not affect OA-enhanced NF-kappaB transcriptional potency. 5 and 10 μM SB203580 enhanced rather than inhibited NF-kappaB-mediated promoter activity by 2 fold [3].

体内活性

SB203580 improved renal function by decreasing the levels of proteinuria and serum BUN, ameliorating the pathologic changes of kidney and reducing Ig and C(3) depositions in the kidney. Hepatocytes necrosis, recruitment and proliferation of leucocytes in liver and spleen were found to be inhibited by administration of SB203580 [4]. Compared with placebo, high dose SB203580 (100 mg/kg) pretreatment increased the hazards ratio of death. Decreasing doses (10, 1, or 0.1 mg/kg) went from being harmful to having no significant effect. At 48 hours, but not 24 hours after E. coli, high and low dose SB203580 pretreatment decreased cardiac phosphorylated p38 MAPK levels and improved cardiac output either. Low dose SB203580 did not alter lung neutrophils significantly but increased lung injury at 48 hours. High dose decreased lung neutrophils and injury at 24 hours but then increased them at 48 hours [5].

动物实验

In survival studies, C57BL/6J mice weighing 20 g to 30 g were briefly anesthetized with isoflurane and challenged with 0.05 mL of IT normal saline (NS, noninfected controls) or E. coli (15 × 10^9 CFU/kg) as previously described. One hour before NS challenge, mice (n = 24) received either intraperitoneal SB203580 (100 mg/kg in 0.25 mL) or diluent only (placebo). Infected animals received SB203580 in doses of 100, 10, 1, or 0.1 mg/kg or placebo 1 hour before IT E. coli (n = 241); SB203580 100 or 0.1 mg/kg or placebo 1 hour after E. coli (n = 121); or SB203580 100 mg/kg or placebo 12 hours after E. coli (n = 72). All animals received ceftriaxone (100 mg/kg in 0.1 mL, subcutaneously) for 4 days and NS (0.5 mL, subcutaneously) for 1 day beginning 4 hours after challenge. Animals were observed every 2 hours for the initial 48 hours, every 4 hours from 48 hours to 72 hours, every 8 hours from 72 hours to 96 hours, and then twice daily until study completion (168 hours). Sequential weekly experiments with 24 animals each compared either two to three doses of SB203580 versus placebo administered at similar times or similar doses of SB203580 versus placebo at differing treatment times. Study groups in each experiment were of equivalent sample size (i.e., 6 – 8 per group) [5].

细胞实验

The luciferase reporter plasmid pIL6luc(-122) and the CAT reporter plasmid p(TRE)5CAT were transfected into TF-1 cell line by means of electroporation. Prior to transfection, cells were cultured for 16?h at a density of 0.5×10^6 cells/ml in the appropriate medium, washed twice and resuspended in RPMI 1640 at a density of 10×10^6 in 200? μl. When transfected with a single plasmid, 25? μg of DNA was added and the mixture was left at room temperature for 15?min. Cotransfections were performed with 15? μg of the reporter plasmid pIL6luc(-122) together with 15? μg of the dominant-negative expression plasmids (pRSV-MKK3(Ala), pcDNA3-MKK6(K82A), pRSV-N Δ Raf1, pcDNA3-MKK4(Ala), pcDNA3-Flag-JNK1, or pcDNA3 (empty vector). Cotransfections of pGAL4tkluc (5? μg) with either pGAL4p65 (5? μg) or pGAL4dbd (5? μg) were performed under similar conditions. In addition, cells were cotransfected with 2? μg of a CMV-CAT plasmid, to normalize for transfection efficiency. Electroporation, in 0.4?cm electroporation cuvettes, was performed at 240?V and 960? μF with Gene Pulser electroporator. After electroporation, the cells were replated in RPMI 1640 containing 2% FBS. Six hours after transfection cells were stimulated for 24?h with medium or OA (30?ng/ml) or SB203580 for 30?min prior to OA stimulation. The cells were then harvested and lysed by commercially available luciferase lysis buffer. One-hundred μl of lysis product was added to 100? μl of luciferase assay reagents and luciferase activity was measured with the Anthos Lucy1 luminometer. CAT reporter activity of 100? μl lysis product plus 100? μl CAT dilution buffer was determined with a commercially available CAT Elisa kit [3].

描述

Adezmapimod (PB 203580) is a p38 MAPK inhibitor (IC50: 0.3-0.5 μM). It shows more than 100-fold selectivity over PKB, LCK, and GSK-3β.

储存

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

For technical support and original validation data for this product please contact
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