

产品名称：**4-(4-氟苯基)-2-(4-羟基苯基)-5-(4-吡啶基)-1H-咪唑**
 产品别名：**SB 202190**

生物活性:

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| Description | SB 202190 is a cell-permeable p38 MAP kinase inhibitor with IC₅₀s of 50 nM and 100 nM for p38α and p38β2, respectively. SB 202190 binds to the ATP pocket of the active recombinant human p38 kinase with a K_d of 38 nM. | | | | |
| IC ₅₀ & Target | p38α | p38β2 | | | |
| | 50 nM (IC ₅₀) | 100 nM (IC ₅₀) | | | |
| In Vitro | Treatment of cells with SB 202190 (SB202190) significantly inhibits both basal and anti-Fas antibody-induced MAPKAPK 2 activity in a dose-dependent manner as measured in immune complex kinase assays with GST-hsp27 as a substrate. Jurkat cells are treated with SB202190 or left untreated. After 24 h, cells are harvested, and the activity of CPP32-like caspases in cell extracts is measured by cleavage of the fluorescent peptide DEVD-AMC, which is a specific substrate of CPP32-like caspases. The cleavage of DEVD-AMC is significantly increased in cells treated with SB202190 but not in the control[2]. | | | | |
| In Vivo | In HCT-116-derived colorectal tumors, administration of SB 202190 (SB202190), Bay 43-9006 or a combination of both give similar results in terms of measurement of external tumor size (around 58% growth reduction compare with control tumors). SB202190 induces a 28% reduction of tumor growth, compare with a 31% reduction promoted by Bay 43-9006, while combination of both drugs reduce tumor growth by 55%[3]. Compare to the model group, the SB202190 group exhibits significantly shorter escape latencies in the Morris water maze hidden platform trials (P<0.01) and longer times in the original platform quadrant during probe trials (P<0.01). The SB202190 group also shows significantly reduced neuronal apoptosis in the hippocampus compared to VaD model rats (P<0.01) as well as higher (antiapoptotic) Bcl-2 expression and lower (proapoptotic) caspase-3 expression (P<0.01 for both). In conclusion, blockade of the p38 MAPK signaling pathway by SB202190 following permanent 2-OV reduced apoptosis of hippocampal neurons and rescued spatial learning and memory deficits[4]. | | | | |
| Solvent&Solubility | In Vitro: DMSO : ≥ 40 mg/mL (120.72 mM) * "≥" means soluble, but saturation unknown. | | | | |
| | Preparing Stock Solutions | <div>Solvent / Mass / Concentration</div> | 1 mg | 5 mg | 10 mg |
| | | 1 mM | 3.0180 mL | 15.0902 mL | 30.1805 mL |
| | | 5 mM | 0.6036 mL | 3.0180 mL | 6.0361 mL |
| | | 10 mM | 0.3018 mL | 1.5090 mL | 3.0180 mL |
| | *请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。 储备液的保存方式和期限 -80℃, 6 months; -20℃, 1 month。 -80℃ 储存时，请在 6 个月内使用，-20℃ 储存时，请在 1 个月内使用。 In Vivo: 请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂： ——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出 | | | | |

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| | <p>现沉淀、析出现象，可以通过加热和/或超声的方式助溶</p> <p>1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline Solubility: ≥ 2.08 mg/mL (6.28 mM); Clear solution</p> <p>此方案可获得 ≥ 2.08 mg/mL (6.28 mM, 饱和度未知) 的澄清溶液。</p> <p>以 1 mL 工作液为例，取 100 μL 20.8 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。</p> <p>2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.08 mg/mL (6.28 mM); Clear solution</p> <p>此方案可获得 ≥ 2.08 mg/mL (6.28 mM, 饱和度未知) 的澄清溶液。</p> <p>以 1 mL 工作液为例，取 100 μL 20.8 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。</p> <p>3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: 2.08 mg/mL (6.28 mM); Clear solution</p> <p>此方案可获得 ≥ 2.08 mg/mL (6.28 mM, 饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。</p> <p>以 1 mL 工作液为例，取 100 μL 20.8 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。</p> |
| References | <p>[1]. Davies SP, et al. Specificity and mechanism of action of some commonly used protein kinase inhibitors. <u>Biochem J. 2000 Oct 1;351(Pt 1):95-105.</u></p> <p>[2]. Nemoto S, et al. Induction of apoptosis by SB202190 through inhibition of p38β mitogen-activated protein kinase. <u>J Biol Chem. 1998 Jun 26;273(26):16415-20.</u></p> <p>[3]. Grossi V, et al. Bay 43-9006 inhibits p38α activity in colorectal cancer cells and synergizes with the DFG-in inhibitor SB202190 to increase apoptotic response. <u>Cancer Biol Ther. 2012 Dec;13(14):1471-81.</u></p> <p>[4]. Yang S, et al. Protective effects of p38 MAPK inhibitor SB202190 against hippocampal apoptosis and spatial learning and memory deficits in a rat model of vascular dementia. <u>Biomed Res Int. 2013;2013:215798.</u></p> <p>[5]. Zhang Y, et al. PP2AC Level Determines Differential Programming of p38-TSC-mTOR Signaling and Therapeutic Response to p38-Targeted Therapy in Colorectal Cancer. <u>EBioMedicine. 2015 Nov 19;2(12):1944-56.</u></p> |
| 实验参考： | |
| Cell Assay | <p>Jurkat/neo or Jurkat/bcl-2 cells (10^6 cells) are treated with or without SB202190 (50 μM), PD098059 (50 μM) in the presence or absence of caspase inhibitor benzyloxycarbonyl-Val-Ala-Asp (zVAD)-fluoromethylketone for 24 h. The cells are then harvested in lysis buffer. The lysates are clarified by centrifugation, and the supernatants are used for caspase assays. The caspase activity is measured in a reaction mixture containing 20 μg of cell extracts, 20 μM fluoregenic peptide acetyl-Asp-Glu-Val-Asp-aminomethylcoumarin (DEVD-AMC). Fluorescent AMC product formation is measured at excitation 360 nm, emission 460 nm using a Cytofluor II fluorescent plate reader[2].</p> |
| | <p>Mice[3]</p> <p>Female CD-1 athymic nude mice (6-8 week old) are used. 10×10^6 HT-29 or 10×10^6 HCT-116 cells are injected subcutaneously into the flanks (0.2 mL per flank) of female athymic nude CD-1 mice. The volume of the tumors is measured every 2-3 d. The tumor volume is calculated using the</p> |

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| <p>Animal Administration</p> | <p>following formula: volume (mm³)=(width)²×length×0.5. When the tumor volume reaches 60 mm³, mice are randomized into four treatment groups (n≥6 for each group): vehicle (control), Bay 43-9006 30 mg/kg/d, SB202190 25 μg/kg/d, and Bay 43-9006 30 mg/kg/d plus SB202190 25 μg/kg/d. Drug treatment is given daily by gavage for Bay 43-9006 and intraperitoneally for SB202190. Mice are treated for 12 d and tumor volume and body weight are recorded every 2-3 d. At the end of the treatment, mice are sacrificed and tumors explanted for histologic and immunohistochemical analysis.</p> <p>Rats[4]</p> <p>Specific pathogen-free (SPF) male Wistar rats (3 month old, 250±10 g) are used. The 60 Wistar rats are randomly assigned to the sham-operated group, the VaD model group, and the SB 202190 group (20 animals each) using a random number table. The VaD rat model (n=40) is established by separating and ligating the bilateral carotid artery via two-vessel occlusion (2-VO). For animals of the sham-operated group (n=20), the bilateral carotid artery is separated using the same methods but without ligation. After recovery, animals of the SB 202190 group receive intracerebroventricular (ICV) injection of SB 202190 and both the VaD model and sham-operated groups received ICV injection of equal volume 0.1% DMSO. In each group, eight rats are examined in the Morris water maze to assess spatial learning and memory, six rats are sacrificed and brain sections are prepared for TUNEL staining and Bcl-2/caspase-3 immunohistochemistry, and six rats are sacrificed and tissue homogenates are prepared for Western blot assay of phospho-p38 MAPK expression.</p> |
| <p>Kinase Assay</p> | <p>MAPKAPK 2 assays are performed. Briefly, Jurkat cells are serum-starved for 24 h and then incubated with or without the specific p38 inhibitor SB 202190 for 30 min prior to treatment with anti-Fas mAb (100 ng/mL) for 2 h or left alone as indicated in the figure legends. The cells are harvested in lysis buffer and clarified by centrifugation. Endogenous MAPKAPK 2 is immunoprecipitated with anti-MAPKAPK 2 polyclonal antibody for 3 h at 4°C. The activity of the immune complex is assayed at 30°C for 30 min in 30 μL of kinase buffer in the presence of 1 μM ATP/10 μCi [γ-³²P]ATP (10 Ci/mmol) with GST-hsp27 as a substrate. The reactions are terminated with Laemmli sample buffer. The proteins are resolved by 13% SDS-polyacrylamide gel electrophoresis followed by autoradiography. The phosphorylated proteins are quantitated by a PhosphorImager[2].</p> |
| <p>References</p> | <p>[1]. Davies SP, et al. Specificity and mechanism of action of some commonly used protein kinase inhibitors. <i>Biochem J.</i> 2000 Oct 1;351(Pt 1):95-105.</p> <p>[2]. Nemoto S, et al. Induction of apoptosis by SB202190 through inhibition of p38beta mitogen-activated protein kinase. <i>J Biol Chem.</i> 1998 Jun 26;273(26):16415-20.</p> <p>[3]. Grossi V, et al. Bay 43-9006 inhibits p38α activity in colorectal cancer cells and synergizes with the DFG-in inhibitor SB202190 to increase apoptotic response. <i>Cancer Biol Ther.</i> 2012 Dec;13(14):1471-81.</p> <p>[4]. Yang S, et al. Protective effects of p38 MAPK inhibitor SB202190 against hippocampal apoptosis and spatial learning and memory deficits in a rat model of vascular dementia. <i>Biomed Res Int.</i> 2013;2013:215798.</p> <p>[5]. Zhang Y, et al. PP2AC Level Determines Differential Programming of p38-TSC-mTOR Signaling and Therapeutic Response to p38-Targeted Therapy in Colorectal Cancer. <i>EBioMedicine.</i> 2015 Nov 19;2(12):1944-56.</p> |