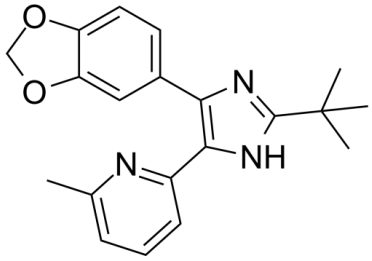
Data Sheet

Product Name:	SB-505124
Cat. No.:	CS-1582
CAS No.:	694433-59-5
Molecular Formula:	C20H21N3O2
Molecular Weight:	335.40
Target:	TGF-β Receptor
Pathway:	TGF-beta/Smad
Solubility:	DMSO : 113.33 mg/mL (337.90 mM; Need ultrasonic)



BIOLOGICAL ACTIVITY:

SB-505124 is a selective inhibitor of **TGF-β Receptor type I receptor** (**ALK4**, **ALK5**, **ALK7**), with **IC_{50}**s of 129 nM and 47 nM for ALK4, ALK5, respectively, but it does not inhibit ALK1, 2, 3, or 6. IC50 & Target: IC50: 129 nM (ALK4), 47 nM (ALK5) **In Vitro:** SB-505124 demonstrates no toxicity to renal epithelial A498 cells at concentrations up to 100 μM for 48 h. 505124 inhibits the closely related ALK4 with an IC_{50} value of 129±11 nM (about 2.5-fold less sensitive than ALK5) but does not inhibit ALK2 at concentrations up to 10 μ M. SB-505124 (1 μM) inhibits the TGF-β-induced phosphorylation of Smad2 in all three of these cell lines in a concentration-dependent fashion. SB-505124 (1 or 5 μM) potently inhibits TGF-β-induced activation of JNK/SAP, extracellular signal-regulated kinase 1/2, and p38 despite the different patterns of activation in these cells[1]. SB-505124 (10 μM) impairs Smad2 phosphorylation and CTGF and α-SMA expression in vitro[2]. SB-505124 susspresses CTGF and α-SMA observed by immunofluorescence. Cell outgrowth from explants dissected from eyes to which SB-505124 is applied during GFS is robust while outgrowth is poor from those treated with MMC[3]. **In Vivo:** SB-505124 (5 mg/kg; i.p.) alone has no effect in C57Bl6 mice with A549 xenografts, but administration of SB-505124 with a single dose of Carboplatin (60 mg/kg) results in durable responses without the need for maintenance therapy in five animals[4].

PROTOCOL (Extracted from published papers and Only for reference)

Kinase Assay: [1]Briefly, phospho-p38 is immunoprecipitated from 200 μg of cell lysates with an immobilized phosphor-p38 antibody overnight at 4°C. p38 kinase activity is measured using 2 μg of ATF-2 fusion protein as the substrate with addition of 200 μM ATP. After a 30-min incubation at 30°C, the reaction is terminated with LaemmLi sample buffer, and the proteins are boiled and resolved by 10% SDS-polyacrylamide gel electrophoresis, transferred to nitrocellulose membrane, and immunoblotted with phospho-ATF-2 antibody. **Cell Assay:** [1]Cell viability is measured as described previously or by using the modified tetrazolium salt WST-1. Approximately 2000 cells are seeded in 96-well dishes in 100 μL of 0.2% FBS phenol red-free media overnight. The cells are treated with 50 μL of SB-505124 (to achieve the final concentrations indicated) for 30 min before being treated with or without TGF-β1 and TNF-α to a final volume of 200 μL. Cell growth is measured at the indicated time points by incubating each well with 10 μL of WST-1 for 3 h at 37°C. Metabolically active cells cleave WST-1 to water-soluble formazan, which is directly quantitated with an enzyme-linked immunosorbent assay plate reader. Each experiment is done at least twice, and treatment for each cell line is done in triplicate.

References:

[1]. DaCosta Byfield S, et al. SB-505124 is a selective inhibitor of transforming growth factor-beta type I receptors ALK4, ALK5, and ALK7. Mol Pharmacol. 2004 Mar;65(3):744-52.

[2]. Sutariya V, et al. Thermoreversible gel for delivery of receptor-like kinase 5 inhibitor SB-505124 for glaucoma filtration surgery. Pharm Dev Technol. 2013

Jul-Aug;18(4):957-62.

[3]. Sapitro J, et al. Suppression of transforming growth factor-β effects in rabbit subconjunctival fibroblasts by receptor-like kinase 5 inhibitor. Mol Vis. 2010 Sep 16;16:1880-92.

[4]. Marini KD, et al. Inhibition of activin signaling in lung adenocarcinoma increases the therapeutic index of platinum chemotherapy. Sci Transl Med. 2018 Jul 25;10(451). pii: eaat3504.

CAIndexNames:

Pyridine, 2-[4-(1,3-benzodioxol-5-yl)-2-(1,1-dimethylethyl)-1H-imidazol-5-yl]-6-methyl-

SMILES:

CC1=CC=CC(C2=C(C3=CC=C(OCO4)C4=C3)N=C(C(C)(C)C)N2)=N1

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