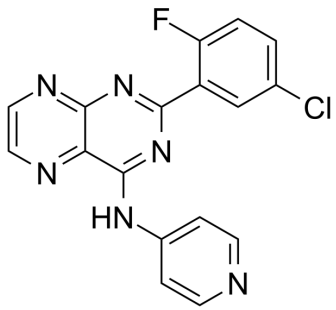
SD-208

Cat. No.:	HY-13227
CAS No.:	627536-09-8
Molecular Formula:	$C_{17}H_{10}ClFN_6$
Molecular Weight:	352.75
Target:	TGF-β Receptor
Pathway:	TGF-beta/Smad
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 9.09 mg/mL (25.77 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.8349 mL	14.1743 mL	28.3487 mL
	5 mM	0.5670 mL	2.8349 mL	5.6697 mL
	10 mM	0.2835 mL	1.4174 mL	2.8349 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: 0.91 mg/mL (2.58 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 0.91 mg/mL (2.58 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 0.91 mg/mL (2.58 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

SD-208 is a selective TGF-βRI (ALK5) inhibitor with IC_{50} of 48 nM, and > 100-fold selectivity over TGF-βRII.

IC_{50} & Target

IC50: 48 nM (TGF-βRI)

In Vitro

SD-208 inhibits the cell growth and constitutive and TGF-beta-evoked migration and invasion, and enhances immunogenicity in murine SMA-560 and human LN-308 glioma cells[1]. SD-208 blocks TGF-beta-induced phosphorylation of the receptor-associated Smads, Smad2 and Smad3, and stimulates epithelial-to-mesenchymal transdifferentiation,

	migration, and invasiveness into Matrigel in vitro[2]. SD-208 also abolishes the promoting effect of TGF-β on neointimal smooth muscle-like cell (SMLC) proliferation and migration in vitro[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	SD-208 (1 mg/mL, p.o.) significantly prolongs the median survival of SMA-560 glioma-bearing mice[1]. In syngeneic 129S1 mice, SD-208 (60 mg/kg/d, p.o.) inhibits primary R3T tumor growth, and reduces the number and the size of lung metastases [2]. In the murine aortic allograft model, SD-208 effectively reduces the formation of intimal hyperplasia of transplant arteriosclerosis (TA)[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	Various kinase activities are assayed by measuring the incorporation of radiolabeled ATP into a peptide or protein substrate. The reactions are performed in 96-well plates and included the relevant kinase, substrate, ATP, and appropriate cofactors. The reactions are incubated and then stopped by the addition of phosphoric acid. Substrate is captured onto a phosphocellulose filter, which is washed free of unreacted ATP. The counts incorporated are determined by counting on a microplate scintillation counter. The ability of SD-208 to inhibit the respective kinase is determined by comparing counts incorporated in the presence of compound with those incorporated in the absence of compound. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [1]	Glioma cells are cultured in the absence or presence of SD-208 (1 μM) for 48 hours. The cells are pulsed for the last 24 hours with [methyl-^{3}H]thymidine (0.5 μCi) and harvested, and incorporated radioactivity is determined in a liquid scintillation counter. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	VM/Dk mice are purchased from the TSE Resource Center. Mice of 6 to 12 weeks of age are used for the survival experiments. Groups of eight mice are anesthesized before all intracranial procedures and placed in a stereotaxic fixation device. A burr hole is drilled in the skull 2 mm lateral to the bregma. The needle of a Hamilton syringe is introduced to a depth of 3 mm. SMA-560 cells [5×10^{3}cells] resuspended in a volume of 2 μL of PBS are injected into the right striatum. Three days later, the mice are allowed to drink SD-208 at 1 mg/mL in deionized water. The mice are observed daily and, in the survival experiments, sacrificed on development of neurologic symptoms. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Rep. 2020 Apr.
- Cell Biol Int. 2020 Mar;44(3):861-872.
- J Clin Transl Hepatol. May 26, 2022.
- Brain Sci. 2021 Jan 8;11(1):77.
- J Mol Neurosci. 2020 Nov;70(11):1728-1741.

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REFERENCES

[1]. Uhl M, et al. SD-208, a novel transforming growth factor beta receptor I kinase inhibitor, inhibits growth and invasiveness and enhances immunogenicity of murine and human glioma cells in vitro and in vivo. Cancer Res. 2004 Nov 1;64(21):7954-61.

[2]. Ge R, et al. Inhibition of growth and metastasis of mouse mammary carcinoma by selective inhibitor of transforming growth factor-beta type I receptor kinase in vivo. Clin Cancer Res. 2006 Jul 15;12(14 Pt 1):4315-30.

[3]. Sun Y, et al. Inhibition of intimal hyperplasia in murine aortic allografts by the oral administration of the transforming growth factor-beta receptor I kinase inhibitor SD-208. J Heart Lung Transplant. 2014 Jun;33(6):654-61.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA