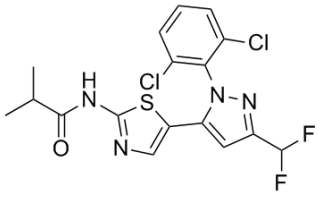
BMS-5

Cat. No.:	HY-18305
CAS No.:	1338247-35-0
Molecular Formula:	$C_{17}H_{14}Cl_2F_2N_4OS$
Molecular Weight:	431.29
Target:	LIM Kinase (LIMK)
Pathway:	Cell Cycle/DNA Damage
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 34 mg/mL (78.83 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3186 mL	11.5931 mL	23.1863 mL
	5 mM	0.4637 mL	2.3186 mL	4.6373 mL
	10 mM	0.2319 mL	1.1593 mL	2.3186 mL

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

BIOLOGICAL ACTIVITY

Description	BMS-5 (LIMKi 3) is a potent **LIMK** inhibitor with **IC_{50}**s of 7 nM and 8 nM for **LIMK1** and **LIMK2**, respectively.
IC_{50} & Target	LIMK1 7 nM (IC_{50}) LIMK2 8 nM (IC_{50})
In Vitro	BMS-5 (LIMKi 3) inhibits cofilin-Ser3 phosphorylation in a dose-dependent manner in $Nf2^{\Delta Ex2}$ mouse Schwann cells (MSCs) with an IC_{50} of ~2 μM. BMS-5 (LIMKi 3) reduces $Nf2^{\Delta Ex2}$ MSC viability in a dose-dependent manner with an IC_{50} of 3.9 μM, but does not significantly reduce the viability of control $Nf2^{flox2/flox2}$ MSCs at equivalent BMS-5 concentrations. At 10 μM BMS-5, $Nf2^{\Delta Ex2}$ MSC viability is 40% compared to 83% for controls[2].
In Vivo	BMS-5 (LIMKi 3) (20 or 200 μM/side) is bilaterally infused into the hippocampus of rats immediately after contextual fear conditioning training. Rats are tested for memory consolidation 48 h after fear conditioning. Post hoc analysis shows that the group treated with 200 μM BMS-5 express lower freezing levels compared to the 20 μM and vehicle

	groups ($P<0.01$)[3].

PROTOCOL

Kinase Assay [1]	The protein kinase domains of human LIMK1 and LIMK2 are expressed as glutathione S-transferase fusion proteins using the Bac-to-Bac system in Sf9 cells. Compounds 1 to 6 (e.g., BMS-5) are assayed for inhibition of LIMK1 and LIMK2 protein kinase activity by radioactive phosphate incorporation into biotinylated full-length human destrin. Reactions are done with a concentration series of compound in 25 mM HEPES, 100 mM NaCl, 5 mM $MgCl_2$, 5 mM $MnCl_2$, 1 μM total ATP, 83 μg/mL biotinylated destrin, 167 ng/mL glutathione S-transferase-LIMK1, or 835 ng/mL glutathione S-transferase-LIMK2 in a total volume of 60 μL at room temperature for 30 min (LIMK1) or 60 min (LIMK2). Reactions are terminated by addition of 140 μL of 20% TCA/100 mM sodium pyrophosphate, and the precipitates are harvested onto GF/C unifilter plates. The radioactivity incorporated is determined using a TopCount after addition of 35 μL Microscint scintillation fluid[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [2]	Cell membrane asymmetry is measured. **$Nf2^{\Delta Ex2}$ MSCs** plated in a 6-well format are incubated with **2 μM BMS-5** or DMSO vehicle for 24 hrs. Cell are harvested and assayed. Plasma membrane asymmetry is evaluated with the Violet ratiometric assay by flow cytometry[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [3]	Rats [3] **Male Wistar rats (age 2-3 months, weight 290-350 g)** are used. BMS-5 is prepared in a vehicle solution (1% DMSO in sterile isotonic saline). At the time of infusion, a 30-gauge infusion needle is fitted into a guide cannula, with its tip protruding 1.0 mm beyond the guide cannula end and aimed at the pyramidal cell layer of CA1 of the dorsal hippocampus. Avolume of **1 μL of BMS-5 (20 and 200 μM)** or vehicle (DMSO 1%) is bilaterally infused in a time of 90 s. The doses of BMS-5 are based on its IC_{50} value and in vitro studies. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Ross-Macdonald P, et al. Identification of a nonkinase target mediating cytotoxicity of novel kinase inhibitors. Mol Cancer Ther. 2008 Nov;7(11):3490-8.

[2]. Petrilli A, et al. LIM Domain Kinases as Potential Therapeutic Targets for Neurofibromatosis Type 2.Oncogene. Oncogene. 2014 Jul 3;33(27):3571-82.

[3]. Lunardi P, et al. Effects of Hippocampal LIMK Inhibition on Memory Acquisition, Consolidation, Retrieval, Reconsolidation, and Extinction. Mol Neurobiol. 2017 Jan 13.

Caution: Product has not been fully validated for medical applications. For research use only.

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