BMS-5

Cat. No.: HY-18305

CAS No.: 1338247-35-0

Molecular Formula: $C_{17}H_{14}Cl_2F_2N_4OS$

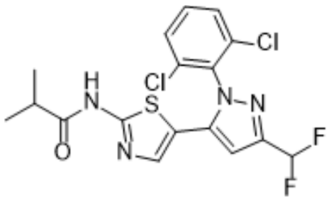
Molecular Weight: 431.29

Target: LIM Kinase (LIMK)

Pathway: Cell Cycle/DNA Damage

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



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.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (4.82 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (4.82 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.82 mM); Clear solution

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	LIMK2
7 nM (IC_{50})	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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

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.

CUSTOMER VALIDATION

- J Virol. 2021 Feb 24;95(10):e02436-20.
- Int J Mol Med. 2021 May;47(5):68.

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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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