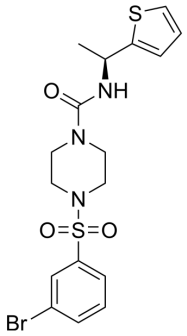
T6167923

Cat. No.:	HY-19744
CAS No.:	2437475-16-4
Molecular Formula:	$C_{17}H_{20}BrN_3O_3S_2$
Molecular Weight:	458.39
Target:	MyD88
Pathway:	Immunology/Inflammation
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 : 250 mg/mL (545.39 mM; Need ultrasonic)

H_2O : < 0.1 mg/mL (ultrasonic;warming;heat to 60°C) (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.1815 mL	10.9077 mL	21.8155 mL
5 mM	0.4363 mL	2.1815 mL	4.3631 mL
10 mM	0.2182 mL	1.0908 mL	2.1815 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 (4.54 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (4.54 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.54 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

T6167923 is a selective inhibitor of MyD88-dependent signaling pathways. T6167923 directly binds to Toll/IL1 receptor (TIR) domain of MyD88 and disrupts MyD88 homodimeric formation. T6167923 inhibits NF-κB driven Staphylococcus enterotoxin AP (SEAP) activity, and improves anti-inflammatory activity with IC_{50}s of 2.7 μM, 2.9 μM, 2.66 μM and 2.66 μM for IFN-γ, IL-1β, IL-6 and TNF-α, respectively[1][2].

IC_{50} & Target

IC50: 2.7 μM (IFN-γ), 2.9 μM (IL-1β), 2.66 μM (IL-6), 2.66 μM (TNF-α)[2]

In Vitro

T6167923 (0-500 μM; 20 h) inhibits the pro-inflammatory cytokine response of staphylococcal enterotoxin B (SEB) in peripheral blood mono nuclear cells[2].
T6167923 (10-500 μM; 2 h) inhibits secreted alkaline phosphatase response (SEAP) expression in HEK 293T cells[2].
T6167923 (100 μM; 16 h) binds to TIR protein and reduced the inhibitory effect on MyD88-signaling[2].
T6167923 (1-500 μM; 13 h) inhibits full-length MyD88 homodimeric formation[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[2]

Cell Line:	Peripheral blood mono nuclear cells
Concentration:	0-500 μM
Incubation Time:	20 hours
Result:	Dose-dependently attenuated the response of SEB to TNF-α, INF-γ, IL-6, and IL-1β with IC_{50}s of 2.66, 2.7, 2.66 and 2.9 μM in peripheral blood mono nuclear cells.

Cell Viability Assay[2]

Cell Line:	HEK 293T cell line
Concentration:	10-500 μM
Incubation Time:	2 hours
Result:	Dose-dependently inhibited lipo-polysaccharide (LPS) induced MyD88-mediated NF-kB driven SEAP expression in HEK 293T cells with IC_{50}s in the range of 40–50 μM.

Cell Viability Assay[2]

Cell Line:	HEK 293T cell line
Concentration:	100 μM
Incubation Time:	16 hours
Result:	Specifically targeted MyD88 and dose-denpendently with TIR protein to reduced the inhibitory effect of MyD88-signaling.

Western Blot Analysis[2]

Cell Line:	HEK 293-I3A cells with MyD88 knockout
Concentration:	1-500 μM
Incubation Time:	13 hours
Result:	Dose-dependently inhibited TIR domain-mediated dimerization of full-length MyD88 and the recombinant TIR domain protein.

In Vivo

T6167923 (0.17 and 1 mg; i.p. once) survives the mice from intoxication with SEB and LPS injection[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	16-20 week-old BALB/c mice with LPS potentiation model[2]
Dosage:	0.17 and 1 mg

Administration:	Intraperitoneal injection; 0.17 and 1 mg once
Result:	Dose-dependently showed a therapeutic efficacy against SEB intoxication.

CUSTOMER VALIDATION

- Signal Transduct Target Ther. 2021 Apr 24;6(1):167.
- Cell Commun Signal. 2024 Jan 5;22(1):16.
- J Med Chem. 2021 May 24.
- Mol Oncol. 2023 Sep 25.
- Int J Cancer. 2024 Jan 30.

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REFERENCES

[1]. Saqib U, et al. Identifying the inhibition of TIR proteins involved in TLR signalling as an anti-inflammatory strategy. SAR QSAR Environ Res. 2018 Apr;29(4):295-318.

[2]. Olson MA, et al. Discovery of small molecule inhibitors of MyD88-dependent signaling pathways using a computational screen. Sci Rep. 2015 Sep 18;5:14246.

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