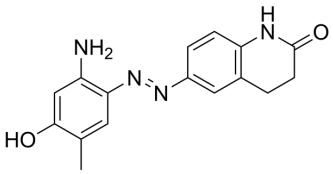
ZL0420

Cat. No.:	HY-112149
CAS No.:	2230496-80-5
Molecular Formula:	$C_{16}H_{16}N_4O_2$
Molecular Weight:	296.32
Target:	Epigenetic Reader Domain
Pathway:	Epigenetics
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 : 125 mg/mL (421.84 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.3747 mL	16.8736 mL	33.7473 mL
	5 mM	0.6749 mL	3.3747 mL	6.7495 mL
	10 mM	0.3375 mL	1.6874 mL	3.3747 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 (7.02 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (7.02 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

ZL0420 is a potent and selective bromodomain-containing protein 4 (BRD4) inhibitor with IC_{50} values of 27 nM against BRD4 BD1 and 32 nM against BRD4 BD2.

IC_{50} & Target

IC50: 27 nM (BRD4 BD1), 32 nM (BRD4 BD2)[1]

In Vitro

ZL0420 is well docked into the acetyl-lysine (KAc) binding pocket of BRD4, forming key interactions including the critical hydrogen bonds with Asn140 directly and Tyr97 indirectly via a H_2O molecule. ZL0420 exhibits submicromolar potency of inhibiting the TLR3-dependent innate immune gene program, including ISG54, ISG56, IL-8, and Groβ genes in cultured human small airway epithelial cells (hSAECs) with IC_{50}s of 0.49-0.86 μM[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo	ZL0420 demonstrates potent efficacy reducing airway inflammation in a mouse model with low toxicity. ZL0420 displays high efficacy and almost completely blocks the profound accumulation of neutrophils around the small and medium sized airways induced by poly(I:C) administration[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	hSAECs are first pretreated with a series final concentrations of BRD4 inhibitors from 0.01 nM to 100 μM for 24 hours and are then added poly(I:C) at 10 μg/mL for another 4 hours prior to harvesting the cells. The harvested cells are first ished with PBS twice and then the total RNA is extracted using acid guanidinium phenol extraction. The total RNA is further reverse-transcribed for gene expression analysis by Q-RT-PCR[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice[1] C57BL/6 mice are pre-treated in the absence or presence of the ZL0420 [10 mg/kg body weight, via the intraperitoneal route] one day prior to poly(I:C) stimulation. The next day, animals are given another dose of ZL0420 immediately followed by intranasal (i.n.) administration of phosphate-buffered saline (PBS, 50 μL) or poly(I:C) (300 μg dissolved in 50 μL PBS). One day later, the mice are euthanized. The bronchoalveolar lavage fluid (BALF) and lung tissues of treated mice are collected for further analysis[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Liu Z, et al. Discovery of potent and selective BRD4 inhibitors capable of blocking TLR3-induced acute airway inflammation. Eur J Med Chem. 2018 May 10;151:450-461.

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