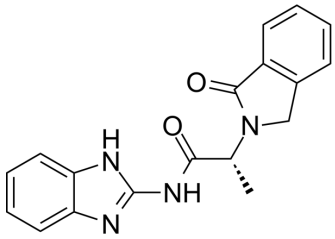
LTβR-IN-1

Cat. No.:	HY-123984
CAS No.:	2189366-77-4
Molecular Formula:	$C_{18}H_{16}N_4O_2$
Molecular Weight:	320.35
Target:	NF-κB
Pathway:	NF-κB
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 : 125 mg/mL (390.20 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.1216 mL	15.6079 mL	31.2159 mL
	5 mM	0.6243 mL	3.1216 mL	6.2432 mL
	10 mM	0.3122 mL	1.5608 mL	3.1216 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 (6.49 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (6.49 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

LTβR-IN-1 is a potent, selective lymphotoxin β receptor (LTβR) inhibitor. LTβR-IN-1 also selectively inhibits the nuclear translocation of p52 depended on TNF12A, instead of the nuclear translocation of p65 mediated by TNF-α receptor. LTβR-IN-1 regulates the NF-kB signaling pathway IN a ligand-independent manner[1].

IC_{50} & Target

LTβR; p52 translocation; MAP3K14; NF-κB[1]

In Vitro

LTβR-IN-1 (compound 919278) (1 nM-100 μM; 30 min) inhibits p52 nuclear translocation in response to stimulation with Anti-LTβR or TWEAK (20 ng/mL, respectively; 4 h) with IC_{50}s of 0.169 μM and 0.167 μM, respectively[1].
LTβR-IN-1 (3 nM-30 μM; 45 min) reduces the binding affinities of both CDK12 and its associated protein, CCNK in both TWEAK-stimulated and control U-2 OS cells, with IC_{50}s of 50-61 nM for CDK12 and 29-68 nM for CCNK, respectively[1].

LTβR-IN-1 reduces the mRNA abundance of MAP3K14 in with an IC_{50} value of 0.32 μM in U-2 OS cells[1].
LTβR-IN-1 (1-10 μM; 30 min) decreases the phosphorylation of serine-2 (Ser2) on the C-terminal domain (CTD) of RNA polymerase (Pol) II[1].
LTβR-IN-1 regulates the noncanonical pathway in a ligandindependent manner and selectively inhibits the noncanonical pathway while sparing the canonical NF-kB signaling pathway[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[1]

Cell Line:	U-2 OS cells
Concentration:	1 μM, 3 μM, and 10 μM
Incubation Time:	30 min
Result:	Reduced the phosphorylating of Ser2 in cells stimulated by 20 ng/mL TWEAK for 4 hr. Note: CDK12 activated RNA Pol II–mediated transcription by phosphorylating Ser^2 within the 52 heptad (Y1S2P3T4S5P6S7) repeats in the C-terminal domain (CTD) of RNA Pol II. Ser ^{2} phosphorylation aids in the release of paused RNA Pol II from promoters, resulting in transcriptional elongation, which is particularly important for the transcription of some long, complex genes.

REFERENCES

[1]. Henry KL, et al. CDK12-mediated transcriptional regulation of noncanonical NF-κB components is essential for signaling. Sci Signal. 2018 Jul 31;11(541).

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