Rheb inhibitor NR1

Cat. No.: HY-124798

CAS No.: 2216763-38-9

Molecular Formula: $C_{25}H_{19}BrCl_2N_2O_3S$

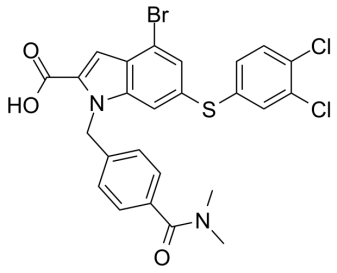
Molecular Weight: 578.3

Target: mTOR

Pathway: PI3K/Akt/mTOR

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 : 50 mg/mL (86.46 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7292 mL	8.6460 mL	17.2921 mL
	5 mM	0.3458 mL	1.7292 mL	3.4584 mL
	10 mM	0.1729 mL	0.8646 mL	1.7292 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: ≥ 2.5 mg/mL (4.32 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Rheb inhibitor NR1 is a Rheb inhibitor with an IC_{50} of 2.1 μM in the Rheb-IVK assay. Rheb inhibitor NR1 can directly bind Rheb in the switch II domain and selectively inhibit the activation of mechanistic target of rapamycin complex 1 (mTORC1). Rheb inhibitor NR1 inhibits the phosphorylation of mTORC1 driven ^{T389}pS6K1 and increases the phosphorylation of ^{S473}pAKT in a dose-dependent manner. Rheb inhibitor NR1 does not influence mTORC2 activity[1].
(Rheb-IVK: Rheb-dependent mTORC1 kinase activity)

IC_{50} & Target

Rheb, mTORC1[1]

In Vitro

NR1 (1-10 μM; 48 h) reduces the size of Jurkat cells[1].
NR1 (0.37-30 μM; 90 min for MCF-7 and TRI102; 24 h for PC3) inhibits the phosphorylation of ^{T389}pS6K1 and increases the phosphorylation of ^{S473}pAKT in MCF-7, TRI102 and PC3 cells[1].
NR1 (1-30 μM; 2.5 h) reduced protein synthesis in MCF-7[1].

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

Cell Viability Assay[1]

Cell Line:	Jurkat cells
Concentration:	1, 3 and 10 μM
Incubation Time:	48 h
Result:	Effectively reduced the size of Jurkat cells in a dose-dependent manner.

Western Blot Analysis[1]

Cell Line:	MCF-7, TRI102 and PC3 cells
Concentration:	0.37, 1.1, 3.3, 10 and 30 μM
Incubation Time:	90 min for MCF-7 and TRI102; 24 h for PC3
Result:	Inhibited the phosphorylation of ^{T389}pS6K1 and increased the phosphorylation of ^{S473} pAKT in a dose-dependent manner.

Western Blot Analysis[1]

Cell Line:	MCF-7
Concentration:	1, 3, 10 and 30 μM
Incubation Time:	2.5 h (then labeled the cells with an ^{35}S-Met labeling mix for 30 min)
Result:	Dose-dependently reduced protein synthesis.

In Vivo

NR1 (30 mg/kg; IP; single dosage) significantly reduces mTORC1 activity in both kidney and skeletal muscle, and exhibited a clear band shift for $^{T37/46}$4E-BP1 in skeletal muscle[1].

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

Animal Model:	Male C57BL/6 mice (6-7 weeks; fast for 16 hours)[1]
Dosage:	30 mg/kg
Administration:	IP; single dosage
Result:	Sustained over 5 μM for 2 h. Significantly reduced mTORC1 activity in both kidney and skeletal muscle, and exhibited a clear band shift for $^{T37/46}$4E-BP1 in skeletal muscle.

CUSTOMER VALIDATION

- PLoS Pathog. 2023 Feb 3;19(2):e1011126.

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REFERENCES

[1]. Mahoney SJ, et al. A small molecule inhibitor of Rheb selectively targets mTORC1 signaling. Nat Commun. 2018 Feb 7;9(1):548.

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