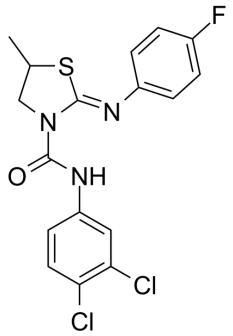
JR-AB2-011

Cat. No.:	HY-122022
CAS No.:	2411853-34-2
Molecular Formula:	$C_{17}H_{14}Cl_2FN_3OS$
Molecular Weight:	398.28
Target:	mTOR
Pathway:	PI3K/Akt/mTOR
Storage:	4°C, protect from light * In solvent : -80°C, 6 months; -20°C, 1 month (protect from light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 62.5 mg/mL (156.92 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.5108 mL	12.5540 mL	25.1080 mL
	5 mM	0.5022 mL	2.5108 mL	5.0216 mL
	10 mM	0.2511 mL	1.2554 mL	2.5108 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 (5.22 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (5.22 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

JR-AB2-011 is a selective mTORC2 inhibitor with an IC_{50} value of 0.36 μM. JR-AB2-011 inhibits mTORC2 activity by blocking Rictor-mTOR association (K_i: 0.19 μM)[1].JR-AB2-011 decreases the phosphorylation level of Akt, decreases MMP2 activity, thereby reducing the ability of tumor cells to migrate and invade. JR-AB2-011 also induces non-apoptotic cell death[2].

IC_{50} & Target

mTORC2
0.36 μM (IC_{50})

In Vitro

JR-AB2-011 (10 μM - 250 μM; 48h) significantly reduces the survival rate and proliferation ability of different melanoma cell lines (MelJu, MelJuso, MelIm, B16)[2].
JR-AB2-011 (50 μM, 250 μM; 48 h) decreases the phosphorylation level of Akt in MelIm cells, indicating that inhibition of mTORC2 attenuated the Ak t signaling pathway[2].

JR-AB2-011 (50 μM, 250 μM; 48-78 h) results in a significant decrease in cell survival fraction SF and a significant reduction in the migration and invasive ability of melanoma cells, which is mainly achieved by decreasing MMP2 activity[2].

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

Western Blot Analysis[2]

Cell Line:	MelJuso
Concentration:	50 μM, 250 μM
Incubation Time:	72h
Result:	JR-AB2-011 significantly reduced MMP2 protein and inhibited MMP2 activity, thereby inhibiting tumor cell invasion.

In Vivo

JR-AB2-011 (20 mg/kg; i.p.; daily) reduces the size and number of liver metastases in C57BL/6N mice with injection of B16 cells. No severe side effects or weight loss[2].

JR-AB2-011 (4 mg/kg; p.o.; daily) significantly blocks the Dioscin-induced promotion of M2 macrophage polarization[3].

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

Animal Model:	C57BL/6N mice with injection of B16 cells [2].
Dosage:	20 mg/kg everyday
Administration:	i.p.
Result:	JR-AB2-011 resulted in a significant decrease in hepatic tumor burden and metastasis load, as assessed by MRI and BLI. Histological analysis confirmed the presence of fewer and smaller metastases in the liver of treated mice. MMP2 expression was also significantly reduced.

Animal Model:	DSS (dextran sulfate sodium) induced colitis in mice [3]
Dosage:	4 mg/kg; Dioscin 160 mg/kg; daily
Administration:	p.o.
Result:	JR-AB2-011 significantly blocked the Dioscin-induced promotion of M2 macrophage polarization. JR-AB2-011 inhibited the mTORC2/PPAR-γ signaling pathway, attenuating the regulatory effects of Dioscin on macrophage metabolism and polarization. The decrease in inflammation-related biomarkers (e.g., TNF-α, IL-6, IFN-γ, etc.) was partially reversed, indicating that the anti-inflammatory effects of Dioscin were suppressed.

CUSTOMER VALIDATION

- Sci Immunol. 2022 Jan 21;7(67):eabj5501.
- J Exp Med. 2023 Oct 2;220(10):e20222056.
- Pharmacol Res. 2021 Jul 31;105796.
- Cell Death Dis. 2022 Feb 3;13(2):107.

- Int J Mol Sci. 2021 Apr 21;22(9):4322.

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REFERENCES

[1]. Zhang A, et al. CCL17 exerts neuroprotection through activation of CCR4/mTORC2 axis in microglia after subarachnoid haemorrhage in rats. Stroke Vasc Neurol. 2022 Jul 26;8(1):4–16.

[2]. Guenzle J, et al. Pharmacological Inhibition of mTORC2 Reduces Migration and Metastasis in Melanoma. Int J Mol Sci. 2020 Dec 22;22(1):30

[3]. Wu M, et al Dioscin ameliorates murine ulcerative colitis by regulating macrophage polarization. Pharmacol Res. 2021 Oct ; 172:105796

Caution: Product has not been fully validated for medical applications. For research use only.

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