MRT199665

Cat. No.: HY-120877

CAS No.: 1456858-57-3

Molecular Formula: $C_{28}H_{31}N_5O_2$

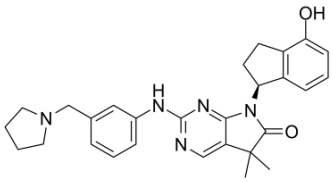
Molecular Weight: 469.58

Target: Salt-inducible Kinase (SIK); AMPK; Apoptosis

Pathway: Immunology/Inflammation; Epigenetics; PI3K/Akt/mTOR; Apoptosis

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 (266.20 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1296 mL	10.6478 mL	21.2956 mL
	5 mM	0.4259 mL	2.1296 mL	4.2591 mL
	10 mM	0.2130 mL	1.0648 mL	2.1296 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 (4.43 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (4.43 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.43 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

MRT199665 is a potent and ATP-competitive, selective MARK/SIK/AMPK inhibitor with IC_{50}s of 2/2/3/2 nM, 10/10 nM, and 110/12/43 nM for MARK1/MARK2/MARK3/MARK14, AMPKα1/AMPKα2, and SIK1/SIK2/SIK3, respectively[1]. MRT199665 causes apoptosis in MEF2C-activated human acute myeloid leukemias (AML) cells[2]. MRT199665 inhibits the phosphorylation of SIK substrate CRTC3 at S370[3].

IC_{50} & Target				
	MARK1	MARK2	MARK3	MARK4
	2 nM (IC_{50})	2 nM (IC_{50})	3 nM (IC_{50})	2 nM (IC_{50})

	SIK1 110 nM (IC_{50})	SIK2 12 nM (IC_{50})	SIK3 43 nM (IC_{50})	NUAK1 3 nM (IC_{50})
	NUAK2 120 nM (IC_{50})	AMPKα1 10 nM (IC_{50})	AMPKα2 10 nM (IC_{50})	MELK 29 nM (IC_{50})
	TBK1 5400 nM (IC_{50})	IKKε 7700 nM (IC_{50})	BRSK2 10000 nM (IC_{50})	

In Vitro

MRT199665 (1 μM; pre-treated for 1 h) increases LPS (100 ng/mL; stimulated for up to 24 h)-stimulated IL-10 mRNA and Nurr77 mRNA production, and IL-10 secretion[1].
MRT199665 (1 nM-100 μM; 48 hours) reduces leukemia growth[2].
MRT199665 treatment can block MEF2C S222 phosphorylation in acute myeloid leukemias (AML) cells.MRT199665 (10 nM-1000 nM; 12 hours) leads to a dose-dependent reduction in total and pS222 MEF2C. MRT199665 also causes a decrease of total MEF2C protein[2].

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

Western Blot Analysis[2]

Cell Line:	OCI-AML2 and MOLM-13 cells
Concentration:	10, 100, 500, and 1000 nM
Incubation Time:	12 hours
Result:	Led to a dose-dependent reduction in total and pS222 MEF2C, causing more than 40% reduction in MEF2C phosphorylation at 10 nM as compared to untreated cells.

Cell Proliferation Assay[2]

Cell Line:	Human AML cell lines OCI-AML2, MV4-11, MOLM-13 and Kasumi-1 with endogenous MEF2C phosphorylation; human AML cell lines NB-4, HEL, HL-60 and U937 lacking MEF2C
Concentration:	1 nM, 10 nM, 100n M, 1 μM, 10 μM, 100μM
Incubation Time:	48 hours
Result:	Human AML cell lines with endogenous MEF2C phosphorylation (OCI-AML2, MV4–11, MOLM-13 and Kasumi-1) were more sensitive as compared to cell lines lacking MEF2C (NB-4, HEL, HL-60 and U937), with mean IC_{50} of 26±13 versus 990±29 nM, respectively.

REFERENCES

[1]. Clark K, et al. Phosphorylation of CRTC3 by the salt-inducible kinases controls the interconversion of classically activated and regulatory macrophages. Proc Natl Acad Sci U S A. 2012 Oct 16;109(42):16986-91.

[2]. Brown FC, et al. MEF2C Phosphorylation Is Required for Chemotherapy Resistance in Acute Myeloid Leukemia. Cancer Discov. 2018 Apr;8(4):478-497.

[3]. Hutchinson LD, et al. Salt-inducible kinases (SIKs) regulate TGFβ-mediated transcriptional and apoptotic responses.Cell Death Dis. 2020 Jan 22;11(1):49.

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

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