SR-3029

Cat. No.: HY-100011

CAS No.: 1454585-06-8

Molecular Formula: $C_{23}H_{19}F_3N_8O$

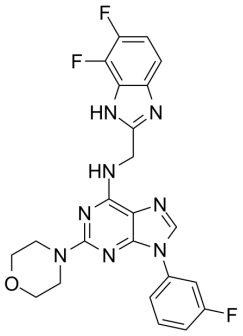
Molecular Weight: 480.45

Target: Casein Kinase

Pathway: Cell Cycle/DNA Damage; Stem Cell/Wnt

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 : ≥ 30 mg/mL (62.44 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.0814 mL	10.4069 mL	20.8138 mL
5 mM	0.4163 mL	2.0814 mL	4.1628 mL
10 mM	0.2081 mL	1.0407 mL	2.0814 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 (4.33 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.33 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

SR-3029 is a potent and ATP competitive CK1δ and CK1ε inhibitor, with IC_{50}s of 44 nM and 260 nM, respectively, and K_is of 97 nM for both kinases.

IC_{50} & Target

CKIδ 44 nM (IC_{50})	CDK6/cyclin D3 427 nM (IC_{50})	CDK6/cyclin D1 428 nM (IC_{50})	CDK4/cyclin D3 368 nM (IC_{50})
CDK4/cyclin D1 576 nM (IC_{50})	FLT3 3000 nM (IC_{50})		

In Vitro	SR-3029 is a potent CK1δ/CK1ε inhibitor, with IC_{50}s of 44 nM and 260 nM, respectively. SR-3029 is ATP competitive, with K_is of 97 nM for CK1δ/CK1ε. SR-3029 also blocks CDK6/cyclin D3, CDK6/cyclin D1, CDK4/cyclin D3, CDK4/cyclin D1 and FLT3, with IC_{50}s of 427, 428, 368, 576, and 3000 nM, respectively. SR-3029 shows inhibitory effects on A375 cells, with an EC_{50} of 86 nM[1] . CK1δ is a necessary and sufficient driver of Wnt/β-catenin signaling in human breast cancer. SR-3029 shows less potent activities against MCF7 and T47D breast cancer cells and the MCF10A cell line, which express low amounts of CK1δ[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	SR-3029 (20 mg/kg daily i.p.) exibits anti-tumor effects in rthotopic MDA-MB-231, MDA-MB-468 (TNBC), SKBR3 and BT474 (HER2+) tumor xenografts with no overt toxicity in mice. SR-3029 (20 mg/kg daily i.p.) also effectively inhibits the growth of tumor in primary patient-derived xenograft (PDX) models. In addition, SR-3029 (20 mg/kg, i.p.) strongly reduces the expression of nuclear β-catenin in tumors of mice[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	Briefly, final assay concentrations for CK1δ, Ulight peptide substrate (ULight-Topo-IIa(Thr1342) peptide) and ATP are 2 nM, 200 nM and 20 μM respectively. The reaction is performed at room temperature in a 10 μL final volume (384-well low volume plate) containing the following: 50 mM Hepes, pH 7.5, 5 mM $MgCl_2$, 0.1 mg/mL bovine serum albumin, 1 mM dl-dithiothreitol, 0.01% Triton X-100 and 1% DMSO. After 10 min, the reaction is terminated by addition of 10 μL of 4 nM Eu-anti-p-Topo-IIa in Lance Detection Buffer. The fluorescent signal is detected using a plate reader. 10 point does-response curves with 3-fold dilutions starting from 10 μM for each compound (SR-3029) is generated in duplicate and data fit to a four parameter logistic [1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [1]	Human A375 melanoma cells are cultured in Dulbecco's Modified Eagle Medium (DMEM) supplemented with 10% fetal bovine serum, 1% penicillin/streptomycin and 1× MEM Non-Essential Amino Acids at 37°C, 5% CO_2. To evaluate the anti-proliferative activity of newly synthesized CK1δ/ε inhibitors, each compound (SR-3029) is subjected to MTT assays against A375 melanoma cells and their EC_{50} values are determined. Briefly, A375 melanoma cells are plated into a 96-well plate and treated with a series of concentrations of each new inhibitor, vehicle (DMSO) or with SR-3029 or SR-1277 (positive controls). MTT assays are performed four days after treatment and data are analyzed using the GraphPad Prism5[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	Stable pools of MDA-MB-231-Luc, MDA-MB-231, MDA-MB-468, SKBR3, or BT474 cells are established by injection of 2×10^6 cancer cells into the mammary fat pads of 6-week-old female athymic nude mice. Establishment of BCM-4013 patient-derived xenografts is performed. Briefly, fresh xenograft tumor fragments (-1 mm^3) are transplanted into the cleared mammary fat pad of recipient SCID/Bg mice. Mice are treated with SR-3029 or vehicle (10:10:80, DMSO:Tween-80:Water) at 20 mg/kg daily by i.p. injection. Tumor volumes are measured as the indicated intervals using calipers or by luminescence imaging with the IVIS 100 imager after subcutaneous injection of luciferin (15 mg/mL). Average radiance (p/s/cm^2/sr) is determined from tumor region-of-interest (ROI) using Living-Image analysis software[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Proc Natl Acad Sci U S A. 2018 Aug 7;115(32):E7522-E7531.
- Research Square Preprint. 2023 Aug 21.

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REFERENCES

[1]. Bibian M, et al. Development of highly selective casein kinase 1δ/1ε (CK1δ/ε) inhibitors with potent antiproliferative properties. Bioorg Med Chem Lett. 2013 Aug 1;23(15):4374-80.

[2]. Rosenberg LH, et al. Therapeutic targeting of casein kinase 1δ in breast cancer. Sci Transl Med. 2015 Dec 16;7(318):318ra202.

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