Centrinone-B

Cat. No.: HY-18683

CAS No.: 1798871-31-4

Molecular Formula: $C_{27}H_{27}F_2N_7O_5S_2$

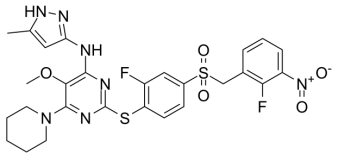
Molecular Weight: 631.67

Target: Polo-like Kinase (PLK)

Pathway: Cell Cycle/DNA Damage

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 : 25 mg/mL (39.58 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.5831 mL	7.9155 mL	15.8311 mL
5 mM	0.3166 mL	1.5831 mL	3.1662 mL
10 mM	0.1583 mL	0.7916 mL	1.5831 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (3.96 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (3.96 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Centrinone-B (LCR-323) is a potent and highly selective PLK4 inhibitor, with a K_i of 0.59 nM.

IC_{50} & Target

PLK4	PLK4 (G95L)	Aurora A	Aurora B
0.59 nM (Ki)	497.53 nM (Ki)	1239 nM (Ki)	5597.14 nM (Ki)

In Vitro

Centrinone-B (LCR-323) is a potent and highly selective PLK4 inhibitor, with a K_i of 0.59 nM. Centrinone-B slightly binds to Aurora A and Aurora B, with K_is of 1239 nM and 5597.14 nM. Centrinone-B (LCR-323) exhibits >1000-fold selectivity for Plk4 over Aurora A/B in vitro and does not affect cellular Aurora A or B substrate phosphorylation at concentrations that deplete centrosomes[1]. Centrinone-B (LCR-323) (0-200 nM) significantly decreases cell viability of PLK4-centriole conjunction melanoma cell lines except p53 mutant SK-MEL-28, and this effect is via inhibition of PLK4. Inhibition of PLK4 by Centrinone-

B (LCR-323) also induces apoptosis in human melanoma cell lines[2].

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

PROTOCOL

Kinase Assay [1]

All kinase assays are performed in white 384-well plates. Plk4 assays use equal volumes of: (1) purified 6xHis-tagged human Plk4 kinase domain (aa 2-275) (expressed in E. coli and purified via Ni-NTA affinity chromatography) in 20 mM Tris pH 7.5, 100 mM NaCl, 10% glycerol, 1 mM DTT; (2) 2X reaction buffer consisting of 50 mM HEPES pH 8.5, 20 mM $MgCl_2$, 1 mM DTT, 0.2 mg/mL BSA, 16 μM ATP, and 200 μM A-A11 substrate (amino acid sequence: TPSDSLIYDDGLS). The Plk4 concentration in the final reaction is 2.5-10 nM with a final pH of 8.0. Inhibitors arrayed in dose response are added from DMSO stocks. Reactions are allowed to proceed for 4-16 hours at 25°C. Detection is performed using ADP-Glo reagent. Luminescence is measured on an Infinite M1000 plate reader. Data are fit using Prism and K_is are calculated from IC_{50} data[1].

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Cell Assay [2]

The effect of centrinone B on melanoma cell line and normal melanocyte viability is determined using the CytoTox-Glo assay. Briefly, cells are counted and plated in a 96-well plate and next day, treated with centrinone B for 48 hours, followed by incubation for 15 min with AAF-Glo substrate (alanyl-alanylphenylalanyl-aminoluciferin), which determines a distinct intracellular protease activity related with cytotoxicity (dead-cell protease) via a luminescent signal. Cell viability is determined by subtracting the luminescent signals of dead cells (due to centrinone B) from total dead cells (after addition of digitonin to lyse remaining viable cells). Data are represented as relative light units (RLU) for viable cells[2].

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CUSTOMER VALIDATION

- EMBO J. 2021 Apr 9;e106798.
- Proc Natl Acad Sci U S A. 2020 Feb 25;117(8):4310-4319.
- EMBO Rep. 2021 Feb 9;e51094.
- Prostate. 2022 Jun;82(9):957-969.
- Division of Mathematics and Natural Sciences of the Georg-August-Universität Göttingen. 2020 Feb.

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REFERENCES

[1]. Wong YL, et al. Cell biology. Reversible centriole depletion with an inhibitor of Polo-like kinase 4. Science. 2015 Jun 5;348(6239):1155-60.

[2]. Denu RA, et al. Centriole Overduplication is the Predominant Mechanism Leading to Centrosome Amplification in Melanoma. Mol Cancer Res. 2018 Jan 12.

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