Centrinone

Cat. No.: HY-18682

CAS No.: 1798871-30-3

Molecular Formula: $C_{26}H_{25}F_2N_7O_6S_2$

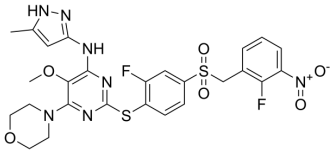
Molecular Weight: 633.65

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 : ≥ 31 mg/mL (48.92 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.5782 mL	7.8908 mL	15.7816 mL
5 mM	0.3156 mL	1.5782 mL	3.1563 mL
10 mM	0.1578 mL	0.7891 mL	1.5782 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 (3.95 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (3.95 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Centrinone (LCR-263) is a selective and reversible inhibitor of polo-like kinase 4 (PLK4) with a K_i of 0.16 nM.

IC_{50} & Target

PLK4	PLK4 (G95L)	Aurora A	Aurora B
0.16 nM (Ki)	68.57 nM (Ki)	171 nM (Ki)	436.76 nM (Ki)

In Vitro

Centrinone (LCR-263) exhibits more than 1000-fold selectivity for Plk4 over Aurora A/B and does not affect cellular Aurora A or B substrate phosphorylation at concentrations that deplete centrosomes. Centrinone (LCR-263) treatment of HeLa human cervical carcinoma cells leads to a progressive reduction in foci containing centriolar and pericentriolar material markers at each round of cell division, until most cells lack centrioles and centrosomes. Treatment with Centrinone (LCR-

263) reduces centriole number in multiciliated Xenopus epithelial cells, which indicates that Plk4 also controls centriole amplification in differentiated cells. Centrinone (LCR-263) treatment causes centrosome depletion in human and other vertebrate cells. Centrosome loss irreversibly arrests normal cells in a senescence-like G1 state by a p53-dependent mechanism that is independent of DNA damage, stress, Hippo signaling, extends mitotic duration, or segregation errors[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]

Purified 6xHis-tagged human Plk4 kinase domain is in 20 mM Tris pH 7.5, 100 mM NaCl, 10% glycerol, 1 mM DTT. 2X reaction buffer consists 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. The Plk4 concentration in the final reaction is 2.5-10 nM with a final pH of 8.0. Inhibitors (Centrinone) array 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 plate reader[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Assay [1]

For each condition, cells are seeded in triplicate into 6-well plates at 50,000 cells/well. 125 nM Centrinone (LCR-263) is added to HeLa cells or 300 nM is added to NIH/3T3 cells. At 24-hour intervals, 3 wells are harvested per condition. Cell counting is performed using a TC10 automated cell counter[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nat Cell Biol. 2019 Dec;21(12):1544-1552.
- Nat Commun. 2019 Apr 18;10(1):1810.
- EMBO J. 2023 Aug 2;e113510.
- EMBO J. 2020 Jan 15;39(2):e102378.
- Curr Biol. 2023 Jan 24;S0960-9822(23)00010-6.

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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.

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