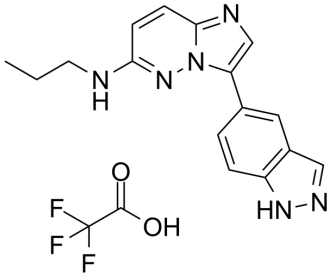
CHR-6494 TFA

Cat. No.:	HY-110350
CAS No.:	1458630-17-5
Molecular Formula:	$C_{18}H_{17}F_3N_6O_2$
Molecular Weight:	406.36
Target:	Haspin Kinase
Pathway:	Cell Cycle/DNA Damage
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	CHR-6494 TFA is a potent inhibitor of haspin, with an IC_{50} of 2 nM. CHR-6494 TFA inhibits histone H3T3 phosphorylation. CHR-6494 TFA induces the apoptosis of cancer cells, including melanoma and breast cancer. CHR-6494 TFA can be used in the research of cancer[1][2][3].
IC_{50} & Target	haspin 2 nM (IC_{50})
In Vitro	CHR-6494 (TFA; 0-10^5 nM; 72 hours) dose-dependently inhibits the growth of cancer cells, such as HCT-116, HeLa, MDA-MB-231, and Wi-38 cells, with IC_{50}s of 500 nM, 473 nM, 752 nM and 1059 nM, respectively[1]. CHR-6494 (TFA; 500 nM) produces a mitotic catastrophe with abnormal morphology of the mitotic spindle and centrosome amplification, and upregulates the spindle assembly checkpoint protein BUB1 and the marker of mitotic arrest cyclin B1[1]. CHR-6494 (TFA; 0, 0.5, 1.0 μM; 24 to 36 h) is an inhibitor of angiogenesis in the ex vivo chicken embryo aortic arch ring assay [1]. CHR-6494 (TFA) exhibits inhibitory activities against melanoma cell lines, including BRAFV600E mutants, NRAS mutants, and wild type cells, with IC_{50}s ranging from 396 nM to 1229 nM[2]. CHR-6494 (TFA; 300 nM and 600 nM; 72 hours) induces apoptosis, increases caspase 3/7 activity by 3- and 6-fold, respectively in COLO-792 cells, and to 8.5- and 16-fold in RPMI-7951 melanoma cells[2]. CHR-6494 (TFA; 50, 200 nM; 1 week) enhances the antiproliferative effects of MLN8237 in MDA-MB-231, SKBR3 breast cancer cells[3]. CHR-6494 (TFA; 200 nM; 72 hours) enhances the apoptosis of MDA-MB-231 and SKBR3 cells when combined with MLN8237[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	CHR-6494 (TFA; 50 mg/kg; i.p. in two cycles of five consecutive days for 15 days) inhibits the growth of tumor in nude mice bearing HCT-116 human colorectal cancer cells[1]. CHR-6494 (TFA; 20 mg/kg; intraperitoneal injection for 15 consecutive days) inhibits the tumor growth in nude mice bearing MDA-MB-231 xenograft tumors[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Male 4-5 weeks old athymic nu/nu mice harboring HCT-116 cells xenograft tumor with a tumor volume of 200 mm^3[1]
Dosage:	50 mg/kg (diluted in a solution of 10% DMSO/20% 2-hydroxypropyl-b-cyclodextrin)

Administration:	i.p. in two cycles of five consecutive days for 15 days
Result:	Dose-dependent tumor growth inhibition was demonstrated. Did not change the body weight of mice.

Animal Model:	4-week-old female nude mice bearing MDA-MB-231 xenograft tumors
Dosage:	20 mg/kg in a final formulation in 10% DMSO/20% 2-hydroxypropyl-β-cyclodextrin
Administration:	i.p. for 15 consecutive days
Result:	Inhibited the tumor volume and weight compared with the control group in nude mice bearing MDA-MB-231 xenograft tumors. Enhanced the tumor volume and weight inhibition of MLN8237 (20 mg/kg; p.o.) in vivo.

CUSTOMER VALIDATION

- Mol Syst Biol. 2018 Aug 13;14(8):e8238.
- Cancer Commun (Lond). 2021 Jan 20.
- J Mol Med (Berl). 2019 Aug;97(8):1183-1193.

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REFERENCES

[1]. Huertas D, et al. Antitumor activity of a small-molecule inhibitor of the histone kinase Haspin. Oncogene. 2012 Mar 15;31(11):1408-18.

[2]. Han L, et al. Anti-Melanoma Activities of Haspin Inhibitor CHR-6494 Deployed as a Single Agent or in a Synergistic Combination with MEK Inhibitor. J Cancer. 2017 Aug 25;8(15):2933-2943.

[3]. Chen A, et al. CRISPR/Cas9 screening identifies a kinetochore-microtubule dependent mechanism for Aurora-A inhibitor resistance in breast cancer. Cancer Commun (Lond). 2021 Feb;41(2):121-139.

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