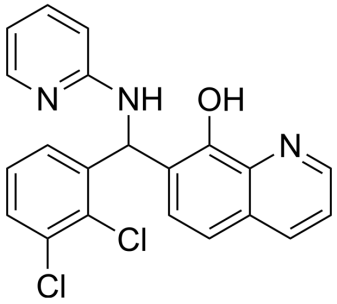
MMRi62

Cat. No.:	HY-148409
CAS No.:	352693-80-2
Molecular Formula:	$C_{21}H_{15}Cl_2N_3O$
Molecular Weight:	396.27
Target:	Ferroptosis; Apoptosis; Autophagy; MDM-2/p53
Pathway:	Apoptosis; Autophagy
Storage:	4°C, protect from light * In solvent : -80°C, 6 months; -20°C, 1 month (protect from light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 62.5 mg/mL (157.72 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.5235 mL	12.6177 mL	25.2353 mL
	5 mM	0.5047 mL	2.5235 mL	5.0471 mL
	10 mM	0.2524 mL	1.2618 mL	2.5235 mL

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

BIOLOGICAL ACTIVITY

Description

MMRi62, a ferroptosis inducer targeting MDM2-MDM4 (negative regulators of tumor suppressor p53). MMRi62 shows a P53-independent pro-apoptotic activity against pancreatic ductal adenocarcinoma (PDAC) cells and induce autophagy. MMRi62 inducesferroptosis, resulting in a increase of reactive oxygen and lysosomal degradation of ferritin heavy chain (FTH1). MMRi62 also leads to proteasomal degradation of mutant p53, also inhibits orthotopic xenograft PDAC mouse model in vivo with high frequency mutation characteristics of KRAS and TP53.12[1][2].

In Vitro

MMRi62 inhibits proliferation, clonogenic, and spheroid growth of pancreatic ductal adenocarcinoma cell (PDAC) by induction of cell death[1].

1MMRi62 (3 nM-100 μM;4 h) binds to RING–RINGheterodimers of MDM2 and MDM4 withthe K_d value of 1.39 μM[2].

MMRi62 (10 nM-1 μM;72 h) induces apoptosis and inhibits leukemic cells with IC_{50}sof 0.34 μM (HL60) and 0.22 μM (HL60VR)[2].

MMRi62 (5 μM and 10μM; 24 h) decreases MDM2B autoubiquitination, increasesMDM4 ubiquitination in a dose-dependent manner[2].

MMRi62 is an E3 ligase modifier capable ofswitching substrate preference from MDM2 to MDM4[2].

MMRi62 (5 μM; 24and 72 h) induces apoptosis in a p53-independent manner[2].

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

Western Blot Analysis[2]

Cell Line:	WT-p53 bearing MV4-11 cells; 293cells transfected with MDM2B and MDM4
Concentration:	2, 2.5, 5, 10, 40, 80, 160 μM
Incubation Time:	24 hours
Result:	Increased cleaved PARP protein and activatedcaspase 3 level in wt-p53 bearing MV4-11 cells at 2 μM for 24 h. Decreased MDM2B autoubiquitination, increasedMDM4 ubiquitination at 5 μM and 10 μM for 24 h. Induced MDM2-dependent degradation of MDM4protein at 5 μM in NALM6 cells.

Cell Proliferation Assay[2]

Cell Line:	Primary AML patient cells, NALM6cells and NALM6shp53 cells
Concentration:	1, 10, 25, and 50 μM
Incubation Time:	24 hours and 72 hours
Result:	Induced NALM6 cells apoptosis at 24 hand induced Primary AML patient cells at 72 h.

In Vivo

MMRi62 shows anti-tumor activity in orthotopic xenograft PDAC mouse models, by inhibiting tumor growth in mice associated with downregulation of NCOA4 and mutant p53[1].
MMRi62 also completely abrogates metastasis of orthotopic tumors[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Li J, et al. Small-Molecule MMRi62 Induces Ferroptosis and Inhibits Metastasis in Pancreatic Cancer via Degradation of Ferritin Heavy Chain and Mutant p53. Mol Cancer Ther. 2022 Apr 1;21(4):535-545.

[2]. Lama R, et al. Small molecule MMRi62 targets MDM4 for degradation and induces leukemic cell apoptosis regardless of p53 status. Front Oncol. 2022 Aug 5;12:933446.

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