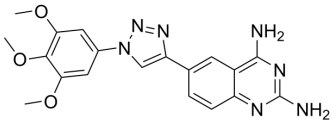
Antitumor agent-81

Cat. No.:	HY-151799
CAS No.:	2765180-17-2
Molecular Formula:	$C_{19}H_{19}N_7O_3$
Molecular Weight:	393.4
Target:	E1/E2/E3 Enzyme; p62
Pathway:	Metabolic Enzyme/Protease; Autophagy
Storage:	4°C, protect from light * In solvent : -80°C, 6 months; -20°C, 1 month (protect from light)



BIOLOGICAL ACTIVITY

Description

Antitumor agent-81 (compound 5a) is a low cytotoxic P62-RNF168 agonist that promotes the interaction of P62 with RNF168. Antitumor agent-81 induces a decrease in RNF168-mediated H2A ubiquitination and impairs homologous recombination-mediated DNA repair. Antitumor agent-81 also inhibits mice xenograft tumor growth in a dose-dependent manner[1].

In Vitro

Antitumor agent-81 (0-20 μM; 72 h) exhibits antiproliferative activity in cells of the most common cancer types[1].
Antitumor agent-81 (1, 2, 5 μM; 24 h) compromises HR (homologous recombination)-mediated DSB repair in HCT-116 cells[1].
Antitumor agent-81 tethers the interaction between P62 and RNF168 in HCT-116 cells[1].
Antitumor agent-81 inhibits the catalytic activity of RNF168 and RNF168 E3 ligase activity in HCT-116 cells[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[1]

Cell Line:	A549, HCT-116, A375, HeLa, HepG2, MCF-7, MDA-MB-231, MGC-803, U2OS and MCF-10A cells
Concentration:	0-20 μM
Incubation Time:	72 h
Result:	Inhibited A549, HCT-116, A375, HeLa, HepG2, MCF-7, MDA-MB-231, MGC-803, U2OS and MCF-10A cells, with IC_{50} values of 1.18, 0.36, 1.93, 2.48, 19.61, 2.79, 1.17, 1.88, 3.64 and 6.98, respectively.

Cell Cycle Analysis[1]

Cell Line:	HCT-116 cells
Concentration:	1, 2, 5 μM
Incubation Time:	24 h
Result:	Induced a G2/M arrest but no significant accumulation of sub-G1 phase. Compromised both HR(homologous recombination)- and NHEJ (non-homologous end joining)- mediated DSB repair in a dose-dependent manner, but HR was the more severely impacted process.

In Vivo

Antitumor agent-81 (5, 10 mg/kg; i.p.; single every 3 days for 22 days) suppresses tumor volumes in a dose-dependent manner in mice[1].

Pharmacokinetic Parameters of Antitumor agent-81 in Female BALB/c nude mice[1].

Dose	$T_{1/2}$ (h)	C_{max} (ng/mL)	AUC_{0-t} (h•ng/mL)	CL ((mL/h)/kg)
IP (5 mg/kg)	16.17	26.10	215.69	19647.83
IP (10 mg/kg)	31.00	39.87	408.18	16554.30
IP (20 mg/kg)	22.10	52.23	1003.58	14669.81

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

Animal Model:	Female BALB/c nude mice (xenograft tumor model)[1].
Dosage:	5, 10 mg/kg
Administration:	Intraperitoneal injection; single every 3 days for 22 days
Result:	Suppressed tumor growth by promoting apoptosis in xenografted tumorigenesis.

Animal Model:	Female BALB/c nude mice[1].
Dosage:	5, 10, 20 mg/kg
Administration:	Intraperitoneal injection; single
Result:	Exhibited plasma concentration peaked 1 h after administration. Showed a relatively high maximum concentration (C_{max}= 52.23 ng/mL) and exposure (AUC_{0-t}= 1003.58 h•ng/mL) at a dose of 20 mg/kg.

REFERENCES

[1]. Wang FC, et al. A 1,2,3-Triazole Derivative of Quinazoline Exhibits Antitumor Activity by Tethering RNF168 to SQSTM1/P62. J Med Chem. 2022 Nov 4.

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