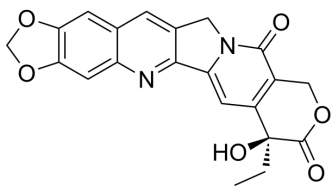
FL118

Cat. No.:	HY-12486
CAS No.:	135415-73-5
Molecular Formula:	$C_{21}H_{16}N_2O_6$
Molecular Weight:	392.36
Target:	Survivin; Apoptosis; IAP
Pathway:	Apoptosis
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 1 mg/mL (2.55 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.5487 mL	12.7434 mL	25.4868 mL
	5 mM	---	---	---
	10 mM	---	---	---

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

BIOLOGICAL ACTIVITY

Description

FL118 (10,11-(Methylenedioxy)-20(S)-camptothecin), a Camptothecin (HY-16560) analogue, is a potent and orally active survivin inhibitor. FL118 binds to oncoprotein DDX5 (p68) to dephosphorylates and degrades DDX5. FL118 can be used for the research of cancer[1][2].

In Vitro

FL118 (0-200 nM; 24, 48 and 72 h) inhibits the cell proliferation of ES-2 and SK-O-V_3 cells[1].
FL118 (0-100 nM; 0 and 24 h) inhibits the migration of ES-2 and SK-O-V_3 cells[1].
FL118 (0-100 nM; 48 h) affects the expression level of cytoglobin (CYGB)[1].
FL118 (10 and 100 nM; 48 h) inhibits PI3K/AKT/mTOR signaling pathway, and affects the expression level of vimentin and E-cadherin in ovarian cancer cells[1].
FL118 (0-100 nM; 6 and 24 h) dephosphorylates and degrades DDX5[2].
FL118 (0-500 nM; 24, 48, 72 h) regulates survivin, McL-1, XIAP, cIAP2, c-MYc and mKras by regulating DDX5[2].
FL118 (0-1 μM, 24 h) shows significant cytotoxic activity against the three tumor cell lines (A549, MDA-MB-231, and RM-1 cells)[3].
FL118 (0-10 nM, 48 h) increases the production of PARP cleavage, and induces apoptosis in A549[3].
FL118 (0-10 nM, 48 h) arrests A549 cells mainly at the G2/M phase[3].

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

Western Blot Analysis[1]

Cell Line:	ES-2 and SK-O-V_3 cell lines
Concentration:	10 and 100 nM
Incubation Time:	48 h
Result:	Effectively inhibited the activation of PI3K/AKT/mTOR signaling pathway in ovarian cancer cells and also inhibited the migration of ES-2 and SK-O-V_3 cells.

Cell Migration Assay [1]

Cell Line:	ES-2 and SK-O-V_3 cell lines
Concentration:	0, 10 and 100 nM
Incubation Time:	0 and 24 h
Result:	Inhibited the migration of ES-2 and SK-O-V_3 cells dose-dependenly.

RT-PCR[1]

Cell Line:	ES-2 and SK-O-V_3 cell lines
Concentration:	0, 10 and 100 nM
Incubation Time:	48 h
Result:	Promoted CYGB expression.

Cell Proliferation Assay[1]

Cell Line:	ES-2 and SK-O-V_3 cell lines
Concentration:	0, 1, 10, 50, 100 and 200 nM
Incubation Time:	24, 48 and 72 h
Result:	Inhibited the cell proliferation of ES-2 and SK-O-V_3 cells time- and dose-dependently.

Western Blot Analysis[2]

Cell Line:	SW620 and Mia Paca-2
Concentration:	0, 10 and 100 nM
Incubation Time:	6 and 24 h
Result:	Induced dephosphorylation of DDX5 through the ubiquitin-proteasome degradation pathway and degraded DDX5 time-dependently.

Western Blot Analysis[2]

Cell Line:	PDAC Panc1, CRC HCT-8, SW620, Mia Paca-2, Panc-1, HCT-8 cell lines
Concentration:	0, 10, 100 and 500 nM
Incubation Time:	24, 48, 72 h

Result:	Controled the expression of survivin, Mcl-1, XIAP, cIAP2, c-Myc and mKras by regulated DDX5, as an upstream master regulator in cancer development and malignant networks.

Cell Cytotoxicity Assay[3]

Cell Line:	A549, MDA-MB-231, RM-1
Concentration:	0-1 μM
Incubation Time:	24 h
Result:	Showed cytotoxicity in A-549 (human lung carcinoma), MDA-MB-231 (human breast carcinoma) and RM-1 (mouse prostate carcinoma), with IC_{50} values of 8.94 ± 1.54 , 24.73 ± 13.82, and 69.19 ± 8.34 nM, respectively.

Apoptosis Analysis[3]

Cell Line:	A549 cells
Concentration:	0, 2.5, 5, 10 nM
Incubation Time:	48 h
Result:	Resulted in the downregulation of survivin. Increased the production of PARP cleavage in a concentration-dependent manner, which is the hallmark of apoptosis. Induced apoptosis in A549.

Cell Cycle Analysis[3]

Cell Line:	A549 cells
Concentration:	0, 2.5, 5, 10 nM
Incubation Time:	48 h
Result:	Increased G2/M cell population in a concentration-dependent manner, and arrested A549 cells mainly at the G2/M phase.

In Vivo

FL118 (5 and 10 mg/kg; p.o. once a week for 20 days) inhibits antitumor activity[1].

FL118 (0-1.5 mg/kg, i.p. once every other day for five times) effectively eliminates human colon and head-and-neck tumors that acquire irinotecan or topotecan resistance[4].

FL118 (1.5 mg/kg, i.v. once) exhibits favorable pharmacokinetics profiles[4].

Pharmacokinetic Parameters of FL118 in female SCID mice[4].

Sample	FaDu	SW620	Plasma
$T_{1/2}$ (hr)	6.852	12.75	1.788
T_{max} (hr)	0.167	0.167	0.167
C_{max} (ng/g, mL)	115	158	43
AUC (hr*ng/g)	413	842	82

AUC_{∞} (hr*ng/g)	448	897	104
AUC% Extrap (%)	7.74	6.17	21.7
Vz (g/kg) (ml/kg)	33052	30742	36849
Cl (g/hr/kg) (ml/hr/kg)	3343	1671	14287

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Animal Model:	Fmale BALB/c nude mice[1]
Dosage:	5 and 10 mg/kg
Administration:	Oral gavage; 5 mg/kg for once a week; 10 mg/kg for once a week; for 20 days
Result:	Showed better antitumor activity than topotecan and dose-dependenly suppressed the growth of ES-2 tumors by upregulating the expression level of CYGB.

Animal Model:	SCID (severe combined immunodeficiency) mice bearing human SW620 (colon) and FaDu (head-and-neck) xenograft tumors (ten-week-old, female, 20-25 g, 5 mice per cage)[4]
Dosage:	0, 0.75, 1, 1.5 mg/kg
Administration:	IP, once every other day for five times as one cycle (If tumors relapse, mice were treated with FL118 for second or third cycles)
Result:	Eliminated human xenograft tumors that acquired irinotecan or topotecan resistance, and was also effective after multiple cycles of treatment without the generation of FL118 resistance.

Animal Model:	SCID (severe combined immunodeficiency) mice bearing human SW620 (colon) and FaDu SCID mice bearing human SW620 (colon) and FaDu (head-and-neck) xenograft tumors (ten-week-old, female, 20-25 g, 5 mice per cage)[4]
Dosage:	1.5 mg/kg
Administration:	IV, once
Result:	Exhibited favorable pharmacokinetics profiles.

REFERENCES

[1]. Zhao H, et al. FL118, a novel anticancer compound, inhibits proliferation and migration of ovarian cancer cells via up-regulation of cytoglobin in vivo and in vitro[J]. Translational Cancer Research, 2017, 6(6):1294-1304.

[2]. Ling X, et al. FL118, acting as a 'molecular glue degrader', binds to dephosphorylates and degrades the oncoprotein DDX5 (p68) to control c-Myc, survivin and mutant Kras against colorectal and pancreatic cancer with high efficacy. Clin Transl Med. 2022 May;12(5):e881.

[3]. Wu G, et al. Synthesis of novel 10,11-methylenedioxy-camptothecin glycoside derivatives and investigation of their anti-tumor effects in vivo. RSC Adv. 2019 Apr 9;9(20):11142-11150.

[4]. Ling X, et, al. FL118, a novel camptothecin analogue, overcomes irinotecan and topotecan resistance in human tumor xenograft models. Am J Transl Res. 2015 Oct 15;7(10):1765-81.

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