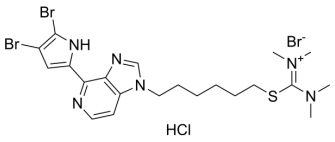
SIRT6-IN-3

Cat. No.:	HY-156027
CAS No.:	3023471-40-8
Molecular Formula:	$C_{21}H_{30}Br_3ClN_6S$
Molecular Weight:	673.73
Target:	Sirtuin; HDAC; Akt; mTOR; Ribosomal S6 Kinase (RSK); ERK
Pathway:	Cell Cycle/DNA Damage; Epigenetics; PI3K/Akt/mTOR; MAPK/ERK Pathway; Stem Cell/Wnt
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

SIRT6-IN-3 (compound 8a) is a selective inhibitor of SIRT6 (IC_{50}=7.49 μM). SIRT6-IN-3 inhibits pancreatic ductal adenocarcinoma (PDAC) cells proliferation and induces apoptosis. SIRT6-IN-3 increases the sensitivity of cancer cells to gemcitabine (HY-17026) via blocking the DNA damage repair pathway. SIRT6-IN-3 is used in pancreatic cancer research[1].

IC_{50} & Target

SIRT1 80.52 μM (IC_{50})	SIRT2 92.21 μM (IC_{50})	SIRT6 7.46 μM (IC_{50})	HDAC3 111.9 μM (IC_{50})
HDAC6 96.77 μM (IC_{50})	HDAC8 102 μM (IC_{50})		

In Vitro

SIRT6-IN-3 (25 μM, 48 h) induces PDAC cell-cycle arrest and apoptosis[1].

SIRT6-IN-3 (25 μM, 72 h) inhibits the proliferation of pancreatic cancer cells by inhibiting signaling pathways[1].

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

Apoptosis Analysis[1]

Cell Line:	PDAC cells
Concentration:	0, 6.25, 12.5, 25 μM
Incubation Time:	48 h
Result:	Increased the percentages of the G0-G1 phase and decreased cyclin D1 expression in a dose-dependent manner.

Western Blot Analysis[1]

Cell Line:	PDAC cells
Concentration:	0, 6.25, 12.5, 25 μM
Incubation Time:	Overnight
Result:	Significantly down-regulated p-mTOR, p-P70S6K, p-AKT, and p-ERK. Inhibited the activity of both mTORC1 and mTORC2.

	Significantly up-regulated the expression of cleaved-PARP, cleaved-Caspase3, and cleaved-Caspase9.

In Vivo

SIRT6-IN-3 (HY-156027; 20 mg/kg for i.p; once every 2 days for 4 weeks) has antitumor effects on tumor mouse model[1].
SIRT6-IN-3 (HY-156027; 20 mg/kg for i.p; once every 2 days for 4 weeks) enhances the antitumor effects of gemcitabine in vivo when in combination with gemcitabine (ratio 2 : 1)[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Tumor mouse model[1]
Dosage:	20 mg/kg (in combination with 10 mg/kg gemcitabine)
Administration:	Intraperitoneal injection (i.p.); Once every 2 days for 4 weeks
Result:	Inhibited the tumor mass 71.3% in mice with combinations of gemcitabine. Greatly increased the expression of apoptosis maker.

REFERENCES

[1]. Song N, et al. Discovery of a pyrrole-pyridinimidazole derivative as novel SIRT6 inhibitor for sensitizing pancreatic cancer to gemcitabine. Cell Death Dis. 2023 Aug 4;14(8):499.

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