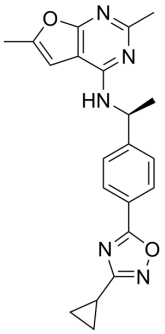
M190S

Cat. No.:	HY-156168
CAS No.:	2578300-07-7
Molecular Formula:	$C_{21}H_{21}N_5O_2$
Molecular Weight:	375.42
Target:	Caspase
Pathway:	Apoptosis
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

M109S is a novel small molecule protecting cells from mitochondria-dependent apoptosis both in vitro and in vivo. M109S has the potential to become a research tool for studying cell death mechanisms and to develop therapeutics targeting mitochondria-dependent cell death pathway. M109S has orally bioactivity with excellent brain permeability[1].

IC_{50} & Target

caspase-3 23.4 nM (EC50)	Caspase 3 23.4 nM (EC50)

In Vitro

M109S (0.1-10000 nM, 24-48 h) inhibits apoptosis induced by Bax as well as Bak[1].
M109S (0-10μM, 4 h) suppresses Staurosporine (HY-15141 STS)-induced apoptosis in MEFs [1].
M109S (0-10μM, 24 h) inhibits Etoposide (HY-13629)-induced apoptosis in Neuro2a cells[1].
M109S (500 nM, 24 h) inhibits Obatoclax (HY-10969A)-induced apoptosis in ARPE19 cells[1].
M109S (500 nM, 48 h) suppresses the conformation change (N-terminal exposure) and mitochondrial translocation of Bax[1].
M109S (1.0 μM, 4h) decreases mitochondrial oxygen consumption and reactive oxygen species, whereas M109S (0.1-1 nM, 4 h) increases glycolysis[1].

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

Apoptosis Analysis[1]

Cell Line:	MEF(Wt, Bax only, Bak only)
Concentration:	0.1 nM, 1 nM, 10 nM, 100 nM, 10000 nM
Incubation Time:	24 h((WT and Bax-only), 48 h (Bak-only)
Result:	Showed a dose-dependent suppression of caspase activation in all three types of MEFs.

Apoptosis Analysis[1]

Cell Line:	MEF
Concentration:	0 nM, 1.6 nM, 8 nM, 40 nM, 200 nM, 10000 nM
Incubation Time:	4 h
Result:	Suppressed STS-induced caspase activation in a dose-dependent manner.

Apoptosis Analysis[1]

Cell Line:	Neuro2a
Concentration:	0 nM, 40 nM, 200 nM, 10000 nM
Incubation Time:	24 h
Result:	Suppressed Etoposide-induced caspase activation in a dose-dependent manner.

Western Blot Analysis[1]

Cell Line:	ARPE19
Concentration:	500 nM
Incubation Time:	24 h
Result:	Significantly inhibited Obatoclax-induced apoptosis in ARPE19 cells comparing to control.

Western Blot Analysis[1]

Cell Line:	iBax cells
Concentration:	500 nM
Incubation Time:	48 h
Result:	Significantly suppressed the amount of immunoprecipitated Bax without a significant change in the total Bax expression.

Immunofluorescence[1]

Cell Line:	iBax cells
Concentration:	500 nM
Incubation Time:	48 h
Result:	Showed the frequency of the punctuated staining was significantly reduced.

In Vivo

M109S (10mg/kg p.o., three time in 48 h) protects the retina from the bright-light-induced photoreceptor death[1].
M109S (1 mg/kg, i.p., i.v., 5 mg/kg, o.p. 10 mg/kg 1 time) is an orally bioactive cell death inhibitor penetrating blood-brain/retina-barrier[1].

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

Animal Model:	$Abca4^{-/-}Rdh8^{-/-}$ mice
Dosage:	10 mg/kg
Administration:	Oral Gavage (p.o.)
Result:	Comparing to mice with M109S, the number of AF spots was similar to that detected in the dark-adapted mice.

Animal Model:	Mice and Rat

Dosage:	Intraperitoneal injection (i.p., 1 mg/kg), Intravenous injection (i.v., 5 mg/kg), or Oral gavage (p.o., 10 mg/kg)
Administration:	Intraperitoneal injection (i.p.), Intravenous injection (i.v.), or Oral gavage (p.o.).
Result:	Showed plasma concentration reached 1.0 mg/mL (2.6 mM) within 30 min from p.o. in mice, and it remained at 596± 134 ng/mL (1.6±0.36 mM) after 24 h, the same as in rat. Plasmic M109S was 565.3±188.3 nM in rats, and 171.0±52.0 nM in retina, 222.7±74.7 nM in brain, respectively.

REFERENCES

[1]. Mieko Matsuyama, et al. Development of novel cytoprotective small compounds inhibiting mitochondria-dependent cell death. Science 26, 107916, October 20, 2023

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