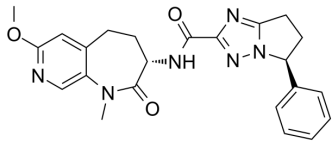
GNE684

Cat. No.:	HY-128585
CAS No.:	2438637-64-8
Molecular Formula:	$C_{23}H_{24}N_6O_3$
Molecular Weight:	432.48
Target:	RIP kinase
Pathway:	Apoptosis
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

GNE684 is a potent inhibitor of potent receptor interacting protein 1 (RIP1), with mean K_i^{app} values of 21 nM, 189 nM and 691 nM for human mouse and rat RIP1, respectively[1].

IC_{50} & Target

IC50: 21 nM (human RIP1), 189 nM (mouse RIP1), 691 nM (rat RIP1)[1]

In Vitro

GNE684 (20 μM; 20 hours) inhibits RIP1 kinase driven cell death effectively in several human and mouse cell lines[1].

GNE684 (20 μM; 0-60 minutes) disrupts TBZ (2 μM BV6, 20 ng/ml TNF, 20 μM zVAD)-induced RIP1 autophosphorylation, interactions between RIP1 and RIP3, RIP3 autophosphorylation, and phosphorylation of MLKL by RIP3[1].

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

Cell Viability Assay[1]

Cell Line:	L929 cells, Jurkat cells, MEFs
Concentration:	20 μM
Incubation Time:	20 hours
Result:	Inhibited RIP1 kinase driven cell death effectively in several human and mouse cell lines.

Western Blot Analysis[1]

Cell Line:	HT-29 cells, J774A.1 cells
Concentration:	0 μM, 20 μM
Incubation Time:	0 minute, 15 minutes, 60 minutes
Result:	Disrupted TBZ (2 μM BV6, 20 ng/ml TNF, 20μM zVAD)-induced RIP1 autophosphorylation, interactions between RIP1 and RIP3, RIP3 autophosphorylation, and phosphorylation of MLKL by RIP3.

In Vivo

GNE684 also had no impact on overall survival or tumor growth in the KPP or KPR (LSL-Kras $^{G12D/+}$; p16/p19 $^{fl/wt}$; Trp53 $^{R270H/wt}$; Pdx1-cre) PDAC models[1].

GNE684 (50mg/kg; p.o. twice daily) inhibits colitis and ileitis caused by NEMO deficiency in intestinal epithelial cells (IECs)[1].

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

Animal Model:	$Nemo^{fl/fl}$ Villin.creERT2 mice (NEMO IEC-KO)[1]
Dosage:	50 mg/kg
Administration:	Oral administration; twice daily; from days 2–6 treated with tamoxifen
Result:	Almost completely protected the NEMO-deficient intestines from colitis and ileitis.

REFERENCES

[1]. Patel S, et al. RIP1 inhibition blocks inflammatory diseases but not tumor growth or metastases. Cell Death Differ. 2019 May 17.

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