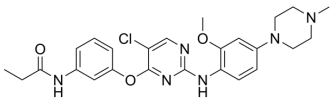
WZ4003

Cat. No.:	HY-15802
CAS No.:	1214265-58-3
Molecular Formula:	$C_{25}H_{29}ClN_6O_3$
Molecular Weight:	496.99
Target:	AMPK
Pathway:	Epigenetics; PI3K/Akt/mTOR
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 1 year -20°C 6 months



SOLVENT & SOLUBILITY

In Vitro

DMSO : 33.33 mg/mL (67.06 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.0121 mL	10.0606 mL	20.1211 mL
	5 mM	0.4024 mL	2.0121 mL	4.0242 mL
	10 mM	0.2012 mL	1.0061 mL	2.0121 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.03 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.03 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

WZ4003 is the first potent and highly specific NUAK kinase inhibitor with IC_{50} of 20 nM/100 nM for NUAK1 (ARK5)/NUAK2, without significant inhibition on other 139 kinases.

IC_{50} & Target

NUAK1	NUAK2
20 nM (IC_{50})	100 nM (IC_{50})

In Vitro

WZ4003 (3-10 μM) markedly suppresses NUAK1-mediated MYPT1 phosphorylation, in HEK-293 cells expressing wild-type NUAK1. Moreover, WZ4003 (10 μM) inhibits MYPT1 Ser445 phosphorylation as well as cell migration, invasion and proliferation to a similar extent as knock out in MEFs or knock down in U2OS cells of NUAK1[1]. WZ4003 also exhibits a high, specific affinity to the L858R/T790M mutant EGFR, while a significantly reduced cellular IC_{50} against T790M containing Ba/F3

cells[2].

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

PROTOCOL

Kinase Assay [1]

In vitro activities of purified GST-NUAK1 and GST-NUAK1[A195T] are measured using Cerenkov counting of incorporation of radioactive ^{32}P from [γ-^{32}P]ATP into Sakamototide substrate peptide. Reactions are carried out in a 50 μL reaction volume for 30 min at 30°C and reactions are terminated by spotting 40 μL of the reaction mix on to P81 paper and immediately immersing in 50 mM orthophosphoric acid. Samples are washed three times in 50 mM orthophosphoric acid followed by a single acetone rinse and air drying. The kinase-mediated incorporation of [γ-^{32}P]ATP into Sakamototide is quantified by Cerenkov counting. One unit of activity is defined as that which catalysed the incorporation of 1 nmol of [^{32}P]phosphate into the substrate over 1 h.

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

Cell Assay [1]

Cell proliferation assays are carried out colorimetrically in 96-well plates. Initially, 2000 cells per well are seeded for U2OS cells and 3000 cells per well are seeded for MEFs. The proliferation assays are carried out over 5 days in the presence or absence of 10 μM HTH-01-015 or WZ4003.

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

CUSTOMER VALIDATION

- Cancer Discov. 2018 May;8(5):632-647.
- J Cell Biol. 2019 Apr 1;218(4):1369-1389.
- Commun Biol. 2021 Mar 25;4(1):399.
- Harvard Medical School LINCS LIBRARY

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REFERENCES

[1]. Banerjee S, et al. Characterization of WZ4003 and HTH-01-015 as selective inhibitors of the LKB1-tumour-suppressor-activated NUAK kinases. Biochem J. 2014 Jan 1;457(1):215-25.

[2]. Zhou W, et al. Novel mutant-selective EGFR kinase inhibitors against EGFR T790M. Nature. 2009 Dec 24;462(7276):1070-4

Caution: Product has not been fully validated for medical applications. For research use only.

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