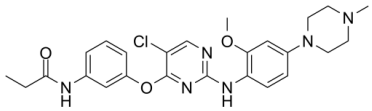
Data Sheet

Product Name:	WZ4003
Cat. No.:	CS-3258
CAS No.:	1214265-58-3
Molecular Formula:	C25H29ClN6O3
Molecular Weight:	496.99
Target:	AMPK
Pathway:	Epigenetics; PI3K/Akt/mTOR
Solubility:	DMSO : 33.33 mg/mL (67.06 mM; Need ultrasonic)



BIOLOGICAL ACTIVITY:

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. IC50 & Target: IC50: 20 nM (NUAK1), 100 nM (NUAK2) **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].

PROTOCOL (Extracted from published papers and Only for reference)

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. **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.

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

CAIndexNames:

Propanamide, N-[3-[[5-chloro-2-[[2-methoxy-4-(4-methyl-1-piperazinyl)phenyl]amino]-4-pyrimidinyl]oxy]phenyl]-

SMILES:

O=C(NC1=CC=CC(OC2=NC(NC3=C(OC)C=C(N4CCN(C)CC4)C=C3)=NC=C2Cl)=C1)CC

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

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