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Lieferung & Zahlungsart

siehe unsere Liefer- und Versandbedingungen

Zuschläge

- Mindermengenzuschlag
- Trockeneiszuschlag
- Gefahrgutzuschlag
- Expressversand

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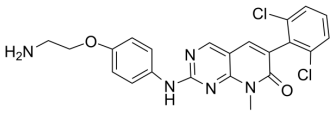
PP58

Cat. No.:	HY-18622
CAS No.:	212391-58-7
Molecular Formula:	$C_{22}H_{19}Cl_2N_5O_2$
Molecular Weight:	456.32
Target:	Src; FGFR; PDGFR
Pathway:	Protein Tyrosine Kinase/RTK
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 62.5 mg/mL (136.97 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.1914 mL	10.9572 mL	21.9144 mL
5 mM	0.4383 mL	2.1914 mL	4.3829 mL
10 mM	0.2191 mL	1.0957 mL	2.1914 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: 2.08 mg/mL (4.56 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

PP58 is a pyrido[2,3-d]pyrimidine-based compound that inhibits PDGFR, FGFR and Src family activities with nanomolar IC_{50} values.

IC_{50} & Target

PDGFR

In Vitro

PP58 inhibits Src with a subnanomolar IC_{50} value in the assays. PP58 behaves as a titration reagent at higher Src protein concentrations. As analyzed by immunoblotting with specific antiserum, the PP58 matrix specifically depletes Src from total lysate, whereas binding to the PP58 beads is prevented when free inhibitor is included. The ectopically expressed FGFR1 receptor tyrosine kinase is specifically retained on PP58 beads. PP58 matrix could be a novel affinity reagent for the purification of cellular pyrido[2,3-d]pyrimidine inhibitor targets. PP58 affinity chromatography leads to the identification of protein kinases belonging to various different groups and families, indicating that the pyrido[2,3-d]pyrimidine inhibitor is not selective for a set of phylogenetically related members of the human kinome. The K_i values of PP58 for p38α and JNK2

	are 3.8±1.9 nM and 0.32±0.04 μM, respectively. PP58 affinity matrix also serves as an efficient purification reagent for a variety of protein kinases, which lack this structural feature and have much lower affinities for the pyrido[2,3-d]pyrimidine inhibitor PP58. PP58 inhibits anisomycin activated p38 in a dose-dependent manner with an IC_{50} below 10 nM. LPS-stimulated TNF-α production is potently inhibited by PP58 with a cellular IC_{50} value of around 3 nM[1]. The T341M mutation abrogates the sensitivity to PP58 inhibition by increasing the cellular IC_{50} value of about 10 nM by more than 1000-fold. The cellular wild-type FGFR1 activity is potently inhibited by low nanomolar concentrations of PP58, whereas dramatic resistance formation is detected for the FGFR1-V561M mutant. PP58 inhibits CSK activity with an IC_{50} value of around 100 nM [2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	PP58 can exhibit some degree of selectivity at low nanomolar concentrations in vivo[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	MEK1 and Aurora A activities are tested at 37 °C in a total volume of 30 μL. The kinases are assayed using 50 μM ATP and 1 μCi [γ-^{32}P]ATP in the presence of different PP58 concentrations. Kinase substrate proteins included are 0.25 mg/mL inactive GST-ERK2 for MEK1 and 0.025 mg/mL kemptide for Aurora A, respectively. Reactions are stopped by addition of SDS sample buffer. Determination of IC_{50} [0–100%] values is performed using GraFit software[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Wissing J, et al. Chemical Proteomic Analysis Reveals Alternative Modes of Action for Pyrido[2,3-d]pyrimidine Kinase Inhibitors. Mol Cell Proteomics. 2004 Dec;3(12):1181-93.

[2]. Blencke S, et al. Characterization of a conserved structural determinant controlling protein kinase sensitivity to selective inhibitors. Chem Biol. 2004 May;11(5):691-701.

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