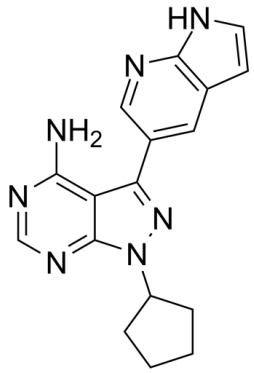
Data Sheet

Product Name:	PP121
Cat. No.:	CS-0087
CAS No.:	1092788-83-4
Molecular Formula:	$C_{17}H_{17}N_7$
Molecular Weight:	319.36
Target:	Apoptosis; mTOR; PDGFR; Src; VEGFR
Pathway:	Apoptosis; PI3K/Akt/mTOR; Protein Tyrosine Kinase/RTK
Solubility:	DMSO : 20 mg/mL (62.63 mM; Need ultrasonic)



BIOLOGICAL ACTIVITY:

PP121 is a multi-targeted kinase inhibitor with **IC_{50}**s of 10, 60, 12, 14, 2 nM for **mTOR**, **DNK-PK**, **VEGFR2**, **Src**, **PDGFR**, respectively. IC50 & Target: IC50: 10 nM (mTOR), 60 nM (DNK-PK), 12 nM (VEGFR2), 14 nM (Src), 2 nM (PDGFR)[1] **In Vitro:** PP121 blocks the PI3K pathway by direct inhibition of PI3K/mTOR in two glioblastoma cell lines, U87 and LN229. PP121 potently inhibits the proliferation of a diverse panel of tumor cell lines containing mutations in the PI3-K pathway components PIK3CA, PTEN, or RAS. PP121 induces a G_0G_1 arrest in most tumor cells. PP121 directly inhibits Src in cells and reverses its biochemical and morphological effects. PP121 potently inhibits the Ret kinase domain in vitro (IC_{50}<1 nM). PP121 potently blocks VEGF stimulated activation of the PI3-K and MAPK pathways. PP121 inhibits VEGFR2 autophosphorylation at low nanomolar concentrations, confirming that this molecule directly targets VEGFR2 in cells. PP121 inhibits Bcr-Abl induced tyrosine phosphorylation in K562 cells as well as BaF3 cells that express Bcr-Abl[1]. **In Vivo:** Oral administration of PP121 remarkably inhibits Eca-109 xenograft growth. Mice body weights are not significantly affected by PP121 or the vehicle treatment. PP121 oral administration dramatically inhibits activations of Akt-mTOR and NFkB in xenograft tumors. p-Akt Ser 473 and p-IKKa/b are both inhibited by PP121 administration[2].

PROTOCOL (Extracted from published papers and Only for reference)

Kinase Assay: [1]Purified kinase domains are incubated with inhibitors (PP121) at 2- or 4-fold dilutions over a concentration range of 50- 0.001 μM or with vehicle (0.1% DMSO) in the presence of 10 μM ATP, 2.5 μCi of γ- ^{32}P-ATP and substrate. Reactions are terminated by spotting onto nitrocellulose or phosphocellulose membranes, depending on the substrate; this membrane is then washed 5-6 times to remove unbound radioactivity and dried. Transferred radioactivity is quantitated by phosphorimaging and IC_{50} values are calculated by fitting the data to a sigmoidal doseresponse using Prism software[1]. **Cell Assay:** PP121 is prepared in 0.1% DMSO[1].Cells grown in 96-well plates are treated with PP121 at 4-fold dilutions (10 μM - 0.040 μM) or vehicle (0.1% DMSO). After 72 h cells are exposed to Resazurin sodium salt (22 μM) and fluorescence is quantified. IC_{50} values are calculated. For proliferation assays involving single cell counting, non-adherent cells are plated at low density (3–5% confluence) and treated with drug (2.5 μM) or vehicle (0.1% DMSO). Cells are diluted into trypan blue daily and viable cells counted using a hemocytometer[1]. **Animal Administration:** PP121 is prepared in 10% 1-methyl-2-pyrrolidinone and 90% PEG 300) group[2].[2]Mouse: Eca-109 cells are injected into the axillary regions of nude mice (5×10^6 cells/mouse). When the tumor volumes reach around 200 mm^3, the mice are randomly separated to three groups: Untreated control, PP121 (30 mg/kg) and vehicle (10% 1-methyl-2-pyrrolidinone and 90% PEG 300) group. Tumor volumes and the mice body weights are measured every 10 d[2].

References:

[1]. Apsel B, et al. Targeted polypharmacology: discovery of dual inhibitors of tyrosine and phosphoinositide kinases. Nat Chem Biol, 2008, 4(11), 691-699.

[2]. Peng Y, et al. The anti-esophageal cancer cell activity by a novel tyrosine/phosphoinositide kinase inhibitor PP121. Biochem Biophys Res Commun. 2015 Sep 11;465(1):137-44.

CAIndexNames:

1H-Pyrazolo[3,4-d]pyrimidin-4-amine, 1-cyclopentyl-3-(1H-pyrrolo[2,3-b]pyridin-5-yl)-

SMILES:

NC1=C2C(C3=CC4=C(N=C3)NC=C4)=NN(C2=NC=N1)C5CCCC5

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