

产品名称：PP121
产品别名：PP121

生物活性:					
Description	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.				
IC ₅₀ & Target	VEGFR2	PDGFR	mTOR	DNK-PK	Src
	12 nM (IC ₅₀)	2 nM (IC ₅₀)	10 nM (IC ₅₀)	60 nM (IC ₅₀)	14 nM (IC ₅₀)
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 ₀ G 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 <i>in vitro</i> (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 NFκB in xenograft tumors. p-Akt Ser 473 and p-IKκa/b are both inhibited by PP121 administration[2].				
Solvent&Solubility	In Vitro: DMSO : 20 mg/mL (62.63 mM; Need ultrasonic)				
	Preparing Stock Solutions	Solvent Mass Concentration	1 mg	5 mg	10 mg
		1 mM	3.1313 mL	15.6563 mL	31.3126 mL
		5 mM	0.6263 mL	3.1313 mL	6.2625 mL
		10 mM	0.3131 mL	1.5656 mL	3.1313 mL
	*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。 储备液的保存方式和期限：-80℃，6 months；-20℃，1 month。-80℃ 储存时，请在 6 个月内使用，-20℃ 储存时，请在 1 个月内使用。 In Vivo: 请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂： ——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶 1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline Solubility: ≥ 2 mg/mL (6.26 mM); Clear solution 此方案可获得 ≥ 2 mg/mL (6.26 mM, 饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 20.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。				

	2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: ≥ 2 mg/mL (6.26 mM); Clear solution 此方案可获得 ≥ 2 mg/mL (6.26 mM, 饱和度未知) 的澄清溶液。 以 1 mL 工作液为例, 取 100 μL 20.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中, 混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2 mg/mL (6.26 mM); Clear solution 此方案可获得 ≥ 2 mg/mL (6.26 mM, 饱和度未知) 的澄清溶液, 此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例, 取 100 μL 20.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中, 混合均匀。
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.
实验参考:	
Cell Assay	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	Mice: 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].
Kinase Assay	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].
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.