产品名称：PF-00562271
产品别名：PF-562271 besylate

生物活性：

Description	PF-562271 besylate is a potent ATP-competitive, reversible inhibitor of FAK and Pyk2 kinase, with an IC50 of 1.5 nM and 13 nM, respectively[1].
IC_{50} & Target	IC50: 1.5 nM (FAK), 13 nM (Pyk2), 30 nM (CDK2), 47 nM (CDK3), 58 nM (CDK1), 97 nM (CDK7), 97 nM (Flt3)[1]
In Vitro	PF-562,271 is a 30- to 120-nM (15.2 to 60.1 ng/mL) inhibitor of cdk2/E, cdk5/p35, cdk1/B, and cdk3/E in recombinant enzyme assays[1]. PF-562,271 blocks bFGF-stimulated blood vessel angiogenesis as performed in chicken chorioallantoic membrane assays[2]. Treatment of cells with PF-562,271 or knock-down of FAK by siRNA is observed to increase cell-cell adhesion strength[3].
In Vivo	PF-562,271 (33 mg/kg, p.o.) inhibits FAK phosphorylation in tumors in a dose- and time-dependent manner in tumor-bearing mice. FAK phosphorylation inhibition relative to total blood concentration of PF-562,271 results in a calculated EC50 of 93 ng/mL. PF-562,271 (25 mg/kg, p.o.) induces apoptosis 2-fold greater in treated tumors compared with vehicle-treated control tumors on day 3[1]. PF-562,271 (33 mg/kg, p.o.) and dasatinib extensively inhibit the movement of tumor cells in the animals. Inhibition of FAK kinase activity following treatment with PF-562,271 results in altered E-cadherin dynamics in vivo[3].
Solvent&Solubility	***In Vitro:*** **DMSO : 21.4 mg/mL (32.15 mM;** Need ultrasonic and warming)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.5023 mL	7.5113 mL	15.0227 mL
5 mM	0.3005 mL	1.5023 mL	3.0045 mL
10 mM	0.1502 mL	0.7511 mL	1.5023 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°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 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: ≥ 1.67 mg/mL (2.51 mM); Clear solution

此方案可获得 ≥ 1.67 mg/mL (2.51 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 16.699999 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: ≥ 1.67 mg/mL (2.51 mM); Clear solution

	此方案可获得 ≥ 1.67 mg/mL (2.51 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 16.699999 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: ≥ 1.67 mg/mL (2.51 mM); Clear solution 此方案可获得 ≥ 1.67 mg/mL (2.51 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 16.699999 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Roberts WG, et al. Antitumor activity and pharmacology of a selective focal adhesion kinase inhibitor, PF-562,271. Cancer Res, 2008, 68(6), 1935-1944. [2]. Lim ST, et al. FERM control of FAK function: implications for cancer therapy. Cell Cycle, 2008, 7(15), 2306-2314. [3]. Canel M, et al. Quantitative in vivo imaging of the effects of inhibiting integrin signaling via Src and FAK on cancer cell movement: effects on E-cadherin dynamics. Cancer Res, 2010, 70(22), 9413-9422.

实验参考：

Animal Administration	Exponentially growing cells are trypsinized and resuspended in sterile PBS and inoculated s.c. (1×10^6 cells per mouse in 200 μL) into the right flank of mice. Animals bearing tumors of appr 150 mm^3 in size are divided into groups receiving either vehicle (5% Gelucire) or PF-562,271 (diluted in vehicle), and dosed by p.o. gavage. Animal body weight and tumor measurements are obtained every 2 d. Tumor volume (mm^3) is measured with Vernier calipers and calculated. For all tumor growth inhibition experiments, 8 to 10 mice per dose group are used. [1]
Kinase Assay	Briefly, purified-activated FAK kinase domain (amino acid 410-689) is reacted with 50 μM ATP and 10 μg per well of a random peptide polymer of Glu and Tyr, p(Glu/Tyr), in kinase buffer [50 mM HEPES (pH 7.5), 125 mM NaCl, and 48 mM $MgCl_2$] for 15 min. Phosphorylation of p(Glu/Tyr) is challenged with serially diluted compound at 1/2-Log concentrations starting at a top concentration of 1 μM. Each concentration is tested in triplicate. Phosphorylation of p(Glu/Tyr) is detected with a general antiphospho-tyrosine (PY20) antibody followed by horseradish peroxidase (HRP)-conjugated goat anti-mouse IgG antibody. HRP substrate is added, and absorbance readings at 450 nm are obtained after addition of stop solution (2mol/LH_2SO_4). IC_{50} values are determined using the Hill-Slope Model. [1]
References	[1]. Roberts WG, et al. Antitumor activity and pharmacology of a selective focal adhesion kinase inhibitor, PF-562,271. Cancer Res, 2008, 68(6), 1935-1944. [2]. Lim ST, et al. FERM control of FAK function: implications for cancer therapy. Cell Cycle, 2008, 7(15), 2306-2314. [3]. Canel M, et al. Quantitative in vivo imaging of the effects of inhibiting integrin signaling via Src and FAK on cancer cell movement: effects on E-cadherin dynamics. Cancer Res, 2010, 70(22), 9413-9422.