产品名称：SU 5402 / 2-[(1,2-二氢-2-氧代-3H-吲哚-3-亚基)甲基]-4-甲基-1H-吡咯-3-丙酸

产品别名：SU 5402

生物活性：

Description	SU 5402 is a potent multi-targeted receptor tyrosine kinase inhibitor with IC_{50} of 20 nM, 30 nM, and 510 nM for VEGFR2, FGFR1, and PDGFRβ, respectively.		
IC_{50} & Target	VEGFR2	FGFR1	PDGFRβ
	20 nM (IC_{50})	30 nM (IC_{50})	510 nM (IC_{50})
In Vitro	SU 5402 is cocrystallized with the catalytic domain of FGF-R1 (flg-1) and is found to inhibit tyrosine phosphorylation of VEGF-R2 (Flk-1/KDR) and PDGF-R in NIH 3T3 cells with IC50 values of 0.4 and 60.9 μM, respectively[1]. In order to investigate whether phosphorylation of PKM2 and LDHA is mediated in FGFR1-specific manner, FTC-133 are treated with receptor tyrosine kinase inhibitors Dovitinib and SU 5402 (SU-5402). Dovitinib treatment results in significant decrease of phosphorylation status at a concentration of 100 nM after four hours of incubation for both PKM2 and LDHA. No significant changes are seen when administered at concentrations of 1 nM and 10 nM. SU 5402 administration leads to a sigificant decrease of PKM2 and LDHA phosphorylation at a concentration of 20 μM[2].		
In Vivo	Inhibition of FGFR1 with SU 5402 (SU5402) administered to ΔF508-CFTR homozygous mice results in partial ΔF508-CFTR rescue, as shown by an increase in saliva secretion, a surrogate "sweat test" assay in mice. As salivary secretion is often sex dependent, only male mice are chosen for these experiments. Our results indicate that treatment of the ΔF508-CFTR mice with SU 5402 restores the saliva secretion level to ~10% of that observed for the wild-type CFTR mice, which suggests that SU 5402 can have therapeutic benefits to Cystic Fibrosis (CF)[3]. The selective FGFR1 inhibitor SU 5402 (SU5402) prevents and/or reverses PH induced by MCT (monocrotaline) in rats. In rats treated with SU 5402 on days 21 to 42 after the MCT injection, evaluations on day 42 show marked decreases in pulmonary artery pressure (PAP), RV/(LV+S), and distal artery muscularization compare with rats treated with the vehicle (saline)[4].		

Solvent&Solubility

In Vitro:

DMSO : ≥ 30 mg/mL (101.24 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.3747 mL	16.8736 mL	33.7473 mL
	5 mM	0.6749 mL	3.3747 mL	6.7495 mL
	10 mM	0.3375 mL	1.6874 mL	3.3747 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: ≥ 2.5 mg/mL (8.44 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (8.44 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 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。
References	[1]. Sun L, et al. Design, synthesis, and evaluations of substituted 3-[(3- or 4-carboxyethylpyrrol-2-yl)methylidenyl]indolin-2-ones as inhibitors of VEGF, FGF, and PDGF receptor tyrosine kinases. J Med Chem. 1999 Dec 16;42(25):5120-30. [2]. Kachel P, et al. Phosphorylation of pyruvate kinase M2 and lactate dehydrogenase A by fibroblast growth factor receptor 1 in benign and malignant thyroid tissue. BMC Cancer. 2015 Mar 18;15:140. [3]. Trzcińska-Daneluti AM, et al. RNA Interference Screen to Identify Kinases That Suppress Rescue of ΔF508-CFTR. Mol Cell Proteomics. 2015 Jun;14(6):1569-83. [4]. Izikki M, et al. Endothelial-derived FGF2 contributes to the progression of pulmonary hypertension in humans and rodents. J Clin Invest. 2009 Mar;119(3):512-23.

实验参考：

Cell Assay	8505C and FTC133 cells are grown in DMEM/F12 suppplemented with 10% FCS and 1% PenStrep and incubated at 37°C, 5% CO2. For B-CPAP RPMI 1640 medium is used. FGFR1 inhibition experiments are performed on FTC133 cells by employment of Receptor Tyrosine Kinase Inhibitors TKI-258 (Dovitinib) and SU 5402 (20μM). Inhibition is conducted over 4 h with the indicated inhibitor concentrations. Control cells receive corresponding concentrations of DMSO[2].
Animal Administration	Mice[3] Male ΔF508 mice (CFTRtm1Eur on a 129/FVB background) and their wild-type littermates of 9-12 weeks are intraperitoneally injected with DMSO or SU 5402 (dissolved in DMSO at the concentration of 6 mg/mL) at 25 mg/kg body weight, every day for 1 week. The mice are weighed daily and the dosages adjusted accordingly. The mice are then anesthetized by inhaling isoflurane until the end of the procedure. Cholinergic antagonist, Atropine (1 mM, 50 μL) is subcutaneously injected into the right cheek to block potential cholinergic stimulation of the salivary gland. A small strip of filter paper is placed against the injected cheek, for 4 min. Isoprenaline (10 mM, 37.5 μL) is subsequently injected in the same spot to stimulate an adrenergic secretion of saliva (time 0). Filter strips (pre-weighed in an Eppendorf tube) are replaced every 5 min, over a period of 30 min. All six filter strips are weighed at the end of the collection and the results are normalized relative to mg/g body weight. Rats[4] To assess the potential effects of the FGFR1 inhibitor SU 5402 on established PH, adult male Wistar rats (200-250 g) are given MCT (60 mg/kg s.c.), left untreated for 21 days, then randomly divided into 2 groups (10 animals in each group), of which one is treated with SU 5402 (25 mg/kg/day) and the other given the vehicle, from day 21 to day 42. All treatments are given once a day by s.c. injection.
	[1]. Sun L, et al. Design, synthesis, and evaluations of substituted 3-[(3- or 4-carboxyethylpyrrol-2-yl)methylidenyl]indolin-2-ones as inhibitors of VEGF, FGF, and PDGF receptor tyrosine kinases. J Med Chem. 1999 Dec 16;42(25):5120-30.

References	[2]. Kachel P, et al. Phosphorylation of pyruvate kinase M2 and lactate dehydrogenase A by fibroblast growth factor receptor 1 in benign and malignant thyroid tissue. BMC Cancer. 2015 Mar 18;15:140. [3]. Trzcińska-Daneluti AM, et al. RNA Interference Screen to Identify Kinases That Suppress Rescue of ΔF508-CFTR. Mol Cell Proteomics. 2015 Jun;14(6):1569-83. [4]. Izikki M, et al. Endothelial-derived FGF2 contributes to the progression of pulmonary hypertension in humans and rodents. J Clin Invest. 2009 Mar;119(3):512-23.