产品名称：TGX-221
产品别名：TGX-221

生物活性：

Description	TGX-221 is a potent, selective, and cell membrane permeable inhibitor of the PI3K p110β catalytic subunit, used for cancer treatment.	
IC_{50} & Target [5]	p110β	p110δ
	8.5 nM (IC_{50})	211 nM (IC_{50})
In Vitro	TGX-221, BL05 and BL05-HA show selective cytotoxicity to LNCaP cells, which may be due to the deficiency of PTEN in this cell line and the accumulation of PIP3 in the cells[1]. TGX-221 (1 μM) does not affect the expression and phosphorylation of AMPK in C2C12 myoblasts[2]. TGX221 (0.1, 1, 10 μM) induces IL-6 release from ASM cells[2]. TGX-221 does not affect neurotensin-stimulated Akt phosphorylation when used alone, but it further suppresses neurotensin-stimulated phosphorylation of Akt when combined with gefitinib. TGX-221 abolishes the neurotensin-stimulated phosphorylation of Akt in Panc-1 cells[3].	
In Vivo	TGX-221 (TGX221, 2.5 mg/kg i.v.) abolishes cyclic flow reductions in a Folts-like carotid artery stenosis preparation of thrombosis, without changing bleeding time, heart rate, blood pressure or carotid vascular conductance[4].	

Solvent&Solubility

In Vitro:

DMSO : 33.33 mg/mL (**91.46 mM;** Need ultrasonic)

H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.7439 mL	13.7197 mL	27.4394 mL
5 mM	0.5488 mL	2.7439 mL	5.4879 mL
10 mM	0.2744 mL	1.3720 mL	2.7439 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 (6.86 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (6.86 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。

2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline)

	Solubility: 2.5 mg/mL (6.86 mM); Suspended solution; Need ultrasonic 此方案可获得 2.5 mg/mL (6.86 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。 以 1 mL 工作液为例，取 100 μL 25.0 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: ≥ 2.5 mg/mL (6.86 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.86 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 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Zhao Y, et al. Prodrug strategy for PSMA-targeted delivery of TGX-221 to prostate cancer cells. Mol Pharm. 2012 Jun 4;9(6):1705-16. [2]. Sturgeon SA, et al. Advantages of a selective beta-isoform phosphoinositide 3-kinase antagonist, an anti-thrombotic agent devoid of other cardiovascular actions in the rat. Eur J Pharmacol. 2008 Jun 10;587(1-3):209-15. [3]. Ge Q, et al. The phosphoinositide 3'-kinase p110δ modulates contractile protein production and IL-6 release in human airway smooth muscle. J Cell Physiol. 2012 Aug;227(8):3044-52. [4]. Chaussade C, et al. Evidence for functional redundancy of class IA PI3K isoforms in insulin signalling. Biochem J. 2007 Jun 15;404(3):449-58. [5]. Müller KM, et al. Role of protein kinase C and epidermal growth factor receptor signalling in growth stimulation by neurotensin in colon carcinoma cells. BMC Cancer. 2011 Oct 2;11:421.

实验参考：

Cell Assay	The prostate cancer cell lines DU145 and LNCaP are maintained in RPMI-1640 medium, and PC3 cells are maintained in F-12K medium. LNCaP is a PSMA positive cell line, whereas DU145 and PC3 are PSMA negative. Both are supplemented with 10 % fetal bovine serum. Cells are plated in 96-well flat-bottomed plates at a concentration of 5,000 cells per well in 90 μL of growth medium. After 12 h, TGX-221, BL05, or BL05-HA loaded micelles in PBS are added at concentrations of 0, 0.1, 1, 5, 10, 50 or 100 μM. PBS and 10 μL of trichloroacetic acid (TCA) are added to negative and positive control wells, respectively. After 72 h, 10 μL of 55-μM resazurin blue is added to each well and incubated at 37°C for 4 h. After incubation, the resorufin product is measured with a fluorophotometer using an excitation wavelength of 560 nm and an emission wavelength of 590 nm. The IC_{50} is determined as the midpoint between positive and negative control groups for each plate using GraphPad Prism 5 software.［1］
Animal Administration	Rats are randomLy assigned to drug treatment groups consisting of the vehicle propylene glycol (0.25 mL/kg), LY294002 (2-(4-morpholinyl)-8-phenyl-4H-1-benzopyran-4-one; a reversible non-specific PI3K inhibitor; 10 mg/kg), wortmannin (an irreversible non-specific PI3K inhibitor; 5 mg/kg), IC87114 (2-[(6-aminopurin- 9-yl)methyl]-5-methyl-3-(2-methylphenyl)quinazolin-4-one; a PI3K p110δ antagonist; 2.5 mg/kg) and the selective PI3K p110β antagonist TGX221 (2.5 mg/kg). In the tail bleeding experiments, rats are randomLy assigned to drug treatment groups consisting of LY294002 (10 mg/kg), IC87114 (2.5 mg/kg), wortmannin (5 mg/kg), TGX221 (2.5 or 25 mg/kg), heparin (100 U/kg), aspirin (2× 200 mg/kg p.o.)± heparin (100 U/kg), and aspirin (2× 200 mg/kg p.o.) combined with heparin (100 U/kg) and TGX221 (2.5 mg/kg). All drugs, with the exception of aspirin,

	are administered as a slow (over ≈45-60 s) i.v. bolus of 0.25 mL/kg into the jugular vein. Aspirin (200 mg/kg suspended in 15% gum arabic in water) is administered twice orally (p.o.)-the first dose is given 24 h before the experiment and the second dose 1 h before the start of the experiment. [4]
References	[1]. Zhao Y, et al. Prodrug strategy for PSMA-targeted delivery of TGX-221 to prostate cancer cells. Mol Pharm. 2012 Jun 4;9(6):1705-16. [2]. Sturgeon SA, et al. Advantages of a selective beta-isoform phosphoinositide 3-kinase antagonist, an anti-thrombotic agent devoid of other cardiovascular actions in the rat. Eur J Pharmacol. 2008 Jun 10;587(1-3):209-15. [3]. Ge Q, et al. The phosphoinositide 3'-kinase p110δ modulates contractile protein production and IL-6 release in human airway smooth muscle. J Cell Physiol. 2012 Aug;227(8):3044-52. [4]. Chaussade C, et al. Evidence for functional redundancy of class IA PI3K isoforms in insulin signalling. Biochem J. 2007 Jun 15;404(3):449-58. [5]. Müller KM, et al. Role of protein kinase C and epidermal growth factor receptor signalling in growth stimulation by neurotensin in colon carcinoma cells. BMC Cancer. 2011 Oct 2;11:421.