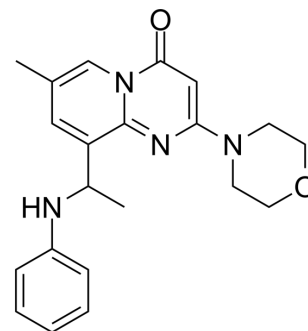


TGX-221

Cat. No.:	HY-10114		
CAS No.:	663619-89-4		
Molecular Formula:	C ₂₁ H ₂₄ N ₄ O ₂		
Molecular Weight:	364.44		
Target:	PI3K		
Pathway:	PI3K/Akt/mTOR		
Storage:	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	6 months
		-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 12.5 mg/mL (34.30 mM; ultrasonic and warming and heat to 60°C)

Concentration	Solvent	Mass		
		1 mg	5 mg	10 mg
Preparing Stock Solutions	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

Please refer to the solubility information to select the appropriate solvent.

In Vivo

- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
Solubility: ≥ 1.25 mg/mL (3.43 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
Solubility: ≥ 1.25 mg/mL (3.43 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil
Solubility: ≥ 1.25 mg/mL (3.43 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

TGX-221 is a potent, selective, and cell membrane permeable inhibitor of the PI3K p110β catalytic subunit, used for cancer treatment.

IC₅₀ & Target

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 μ M) does not affect the expression and phosphorylation of AMPK in C2C12 myoblasts^[2]. TGX221 (0.1, 1, 10 μ M) 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].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

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].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay ^[1]

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 μ L 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 μ M. PBS and 10 μ L of trichloroacetic acid (TCA) are added to negative and positive control wells, respectively. After 72 h, 10 μ L of 55- μ M 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 IC₅₀ is determined as the midpoint between positive and negative control groups for each plate using GraphPad Prism 5 software.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Administration ^[4]

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 p110 δ antagonist; 2.5 mg/kg) and the selective PI3K p110 β 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 \times 200 mg/kg p.o.) \pm heparin (100 U/kg), and aspirin (2 \times 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 \approx 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.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- J Clin Invest. 2021 Dec 15;131(24):e140436.
- Cell Syst. 2020 Jan 22;10(1):66-81.e11.
- Cell Syst. 2020 Jan 22;10(1):66-81.e11.
- EMBO Rep. 2020 Dec 3;21(12):e49756.

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- [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]. Ge Q, et al. The phosphoinositide 3'-kinase p110 δ modulates contractile protein production and IL-6 release in human airway smooth muscle. *J Cell Physiol*. 2012 Aug;227(8):3044-52.
- [3]. 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.
- [4]. 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.
- [5]. 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.
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