产品名称：**TG100-115**
产品别名：**TG100-115**

生物活性：

Description	TG100-115 is a selective PI3Kγ/PI3Kδ inhibitor with IC_{50}s of 83 and 235 nM, respectively.	
IC_{50} & Target	PI3Kγ	PI3Kδ
	83 nM (IC_{50})	235 nM (IC_{50})
In Vitro [1]	TG100-115 inhibits PI3Kγ and PI3Kδ with IC50s of 83 and 235 nM, respectively, whereas both PI3Kα and PI3Kβ are relatively unaffected (IC50 values >1 μM). As a gauge of general specificity, TG100-115 is also assayed against a 133 protein kinase panel, none of which are inhibited at IC50 values <1 μM. TG100-115 potently inhibits edema and inflammation in response to multiple mediators known to participate in myocardial infarction, including vascular endothelial growth factor and platelet-activating factor; by contrast, endothelial cell mitogenesis, a repair process important to tissue survival after ischemic damage[1].	
In Vivo	To correlate these in vivo responses with the molecular target of interest, PI3K pathway signaling is monitored through western blot analyses of Akt phosphorylation (a PI3K-mediated event). VEGF injection i.v. in mice induces a rapid Akt phosphorylation readily detectable in lung lysates, pretreatment with TG100-115 blocks this response. Blockade is seen with TG100-115 doses as low as 0.5 mg/kg and persists over a period of several hours. In initial dose-ranging studies, generally equivalent responses are observed using TG100-115 doses of 0.5-10 mg/kg, and we therefore elected to conduct a statistically powered test at the lowest dose. Animals dosed with TG100-115 as a single 0.5 mg/kg i.v. bolus 30 min after reperfusion developed smaller infarcts vs. vehicle-treated controls. Measuring infarct area as percent of total LV ischemic area, infarct size is reduced by 35% (P=0.04). Viable tissue within the ischemic zone is increased by 37% (P=0.04), directly demonstrating the cardioprotective effect of PI3Kγ/δ inhibition[1].	
Solvent&Solubility	***In Vitro:*** **DMSO： 5.45 mg/mL** (**15.74 mM;** Need ultrasonic and warming)	

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.8873 mL	14.4367 mL	28.8734 mL
	5 mM	0.5775 mL	2.8873 mL	5.7747 mL
	10 mM	0.2887 mL	1.4437 mL	2.8873 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。

References	[1]. Doukas J, et al. Phosphoinositide 3-kinase gamma/delta inhibition limits infarct size after myocardial ischemia/reperfusion injury. Proc Natl Acad Sci U S A. 2006 Dec 26;103(52):19866-71.

实验参考：

Cell Assay	Human umbilical vein EC plated in 96-well cluster plates (5,000 cells/well) are cultured in assay medium (containing 0.5% serum and 50 ng/mL VEGF) in the presence or absence of test compounds (e.g., TG100-115) (10 μM), and cell numbers are quantified by XTT assay 24, 48, or 72 h later[1].
	Rats[1]

Animal Administration	Sprague-Dawley rats (175-200 g) are dosed i.v. with either TG100-115 (1 mg/kg) or vehicle, and 1-4 h later Evans blue dye is administered i.v. as 500 µl of a 2% sterile saline solution. Immediately after dye injection, animals are injected intradermally on each shaved flank with 100 µL of saline, VEGF (2 µg/mL stock), or histamine (10 µg/mL stock). Thirty minutes later, injection sites are photographed.
Kinase Assay	PI3K reactions are constructed by using recombinant human kinases, 3 µM ATP, phosphatidylinositol substrate, and cofactors, and reaction progression measured by using a luminescent-based detection system to quantify ATP consumption. Protein kinase assays are performed by using commercial screening services[1].
References	[1]. Doukas J, et al. Phosphoinositide 3-kinase gamma/delta inhibition limits infarct size after myocardial ischemia/reperfusion injury. Proc Natl Acad Sci U S A. 2006 Dec 26;103(52):19866-71.

源叶生物